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FROSTBITE*

Physiology, Pathology and Therapy

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NEW YORK CITY

THE origin of gangrene subsequent to exposure to cold air or contact cooling has found the most diversified explanations. The general trend of opinions seems to have two different directions. One group, under the leadership of Blackwood[1] and Ungley and his collaborators,[2] attributes most of the damage to a peripheral vasoneuropathy and seems to believe that injury to muscles and other tissues is subsequent to the damage of nerve fibers, which represents the main feature of the disease. Lewis and Love[3] went so far as to attribute most of the damage following frostbite to the bursting of individual cell membranes by the formation of ice crystals. Stimulated by the early studies of Rotnes and Kreyberg[4] another group, consisting of Greene,[5] Siegmund[6] and Friedman,[7] regards the formation of "thrombi" as the cause of gangrene.

FIGURE 1. *Photomicrograph (x 110) of Tissue from an Untreated Rabbit Two Days after Exposure.*

Note the interstitial edema and leukocytic infiltration. All vessels are filled with red-cell masses.

In World War II the casualties due to frostbite were exceedingly numerous. All armies were concerned with this problem, and the number of cases was greatly increased by the severe exposures encountered in high-altitude flying.[8] Damage to the extremities with subsequent gangrene was frequent, and death due to so-called "shock" from

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freezing was not rare. The number of frostbite victims in peacetime is hard to estimate, but in areas may appear, followed by full-blown, self-demarcating, dry gangrene.

FIGURE 2. *Photomicrograph (x 40) of Tissue from an Untreated Rabbit Two Days after Exposure.*
There are hyaline and red-cell masses in the blood vessels.

1943 in New York alone, with its generally mild climate, 14 patients with severe frostbite were admitted to one city hospital. Certain parts of the country have many cases every winter.

PHYSIOLOGY

When a limb is exposed to cold air at temperatures of 0°C. or lower the first reaction is often, although not always, blanching. With continued exposure this is regularly followed by an intense pink color, which, with further cooling, reverts to a cadaverous blanching. This white color persists for some time after the cessation of cooling, depending on the length and severity of the exposure. The next phase, during thawing or warming up, is invariably characterized by an intense red color, a rapid swelling and a rise in the temperature of the limb. Blisters, which are usually present, grow rapidly and may burst within twenty-four to forty-eight hours. The fluid is straw colored or sometimes blood tinged. If the blister persists for more than twenty-four hours it is usually found to contain a dense gelatinous mass, which adheres to the underlying deep-red base. The tissue, especially in the areas of direct exposure, loses all sensation to pinprick, heat and cold, although pressure is usually perceived fairly well, probably because of transmission to adjacent healthy tissues. Within three to ten days, depending on the severity of exposure and individual predisposition, dry, dark-black

If fluorescein tests are performed during such a course of events they illustrate the pathologic physiology in the exposed tissue.

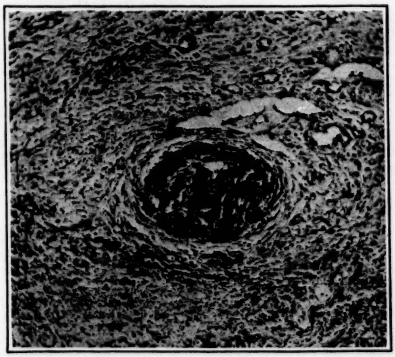

FIGURE 3. *Photomicrograph (x 66) of a Lymphatic Vessel in an Untreated Rabbit Six Days after Exposure.*
This vessel, near the lesion, is clogged with fibrin.

Fluorescein, when injected intravenously, travels with the blood stream and, owing to its small molecule and its negligible electric charge, diffuses

rapidly through the capillary walls. It can be detected wherever it is present by the intense golden-green light that it emits when activated by long-wave ultraviolet light in a dark room. The degree of fluorescence of an area is dependent mainly on the volume of blood reaching the area and on the capillary permeability. After intravenous injection of the dye an even slightly inflamed area will show an intense, golden-green fluorescence, as compared to the pale-green appearance of normal tissue.[9]

A limb of an experimental animal (rabbit) exposed to intense cold by immersion in alcohol at −30°C. for thirty minutes shows a complete absence of fluorescence during, and for approximately an hour after, the exposure. Slowly thereafter the dye starts to reappear in the previously cooled area, and within four hours a repeat fluorescein test reveals a marked hyperfluorescence due to the increased blood flow and to the increase in the permeability of the damaged capillaries. Pressure with a glass spatula on such an area reveals a persistent hyperfluorescence, indicating that the increased amount of dye is in the interstitial space and not only in the blood vessels. Inspection in a normal light discloses marked swelling, heat and reddening of the limb, with bounding pulses. Under the capillary microscope the capillaries show marked dilatation and rapid flow. A fluorescein test, repeated forty-eight to one hundred and forty-four hours later, reveals that the exposed region is again completely nonfluorescent and indicates vascular occlusion with impending gangrene. The same sequence of events can be observed in severe human frostbite.

If the tissues exposed to cold are observed with a capillary microscope a peculiar phenomenon is noted. Just before freezing occurs the red cells are seen to gather into irregular clumps or masses, with plasma in between, until the circulation comes to a complete halt. Immediately after thawing, when the flow starts again, the reverse process takes place, the cells gradually resuming their discreteness. This apparently has no relation to the subsequent formation of occlusive red-cell masses due to excessive transudation of fluid through the hyperpermeable capillary walls. Similar phenomena have been described in malaria and heat injury[10] and in electrical changes of membrane potential.[11] The possible relation to cold agglutinins or other agglutination reactions should be investigated.

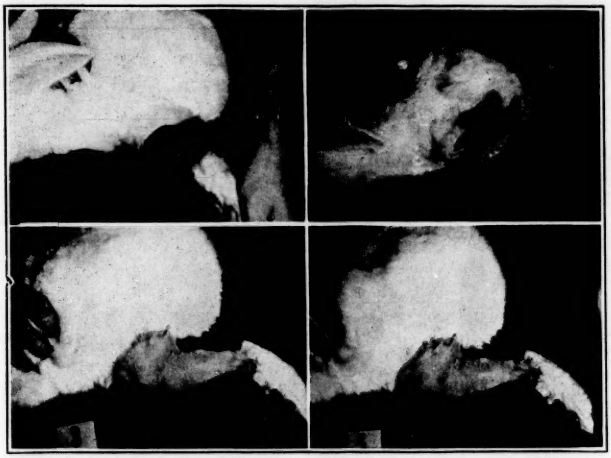

FIGURE 4. *Photographs of Untreated (upper) and Heparinized (lower) Rabbits. The untreated rabbit showed progressing gangrene five days after exposure, and sloughing to the bone ten days later. Three days after exposure there was some swelling of the leg in the heparinized rabbit, with a return to normal five days later.*

PATHOLOGY

Microscopical studies during the phase of increased blood flow reveal that, apparently owing to the fluid loss caused by the increased capillary permeability, the red cells start to silt up the capil-

laries, forming sludge that contains some platelets but little fibrin. These occlusive red-cell masses are not true fibrin thrombi but should be called "agglutinative thrombi"[12] (Fig. 1).* Three to eight days after exposure these agglutinative thrombi start to undergo hyalinization, resulting in completely hyalinized occlusive masses (Fig. 2).

It is interesting to note that, in accordance with the observation of Siegmund,[6] the protein content of all blisters examined while still in the liquid state was almost identical with the plasma protein content of the subject. Within twenty-four to forty-eight hours a dense fibrin clot was formed in every blister. It may be assumed that the same process takes place in the interstitial space and thus gives rise to the subsequent fibrosis and collagenous deposition noted in histologic sections, a process described by Rémy and Thérèse[13] as "lardaceous inflammation." Many lymphatic vessels also show clogging with fibrin deposition (Fig. 3). All this can be attributed to the tremendously increased capillary permeability.[14]

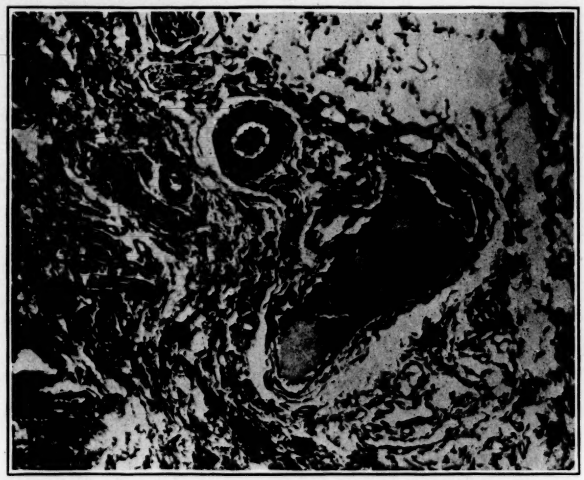

FIGURE 5. *Photomicrograph (x 110) of Tissue from a Heparinized Rabbit Four Days after Exposure.*
The blood vessels are empty or filled with normal content.

THERAPY

Since the gangrene subsequent to frostbite is due to the occlusive red-cell sludge in the capillaries and since some of the damage to muscles and nerves seems to be due to interstitial fibrin deposition leading to fibrosis, it appeared interesting to determine whether heparinization would interrupt the chain of events.

Twenty-one rabbits, exposed to cold by immersion of one of their hind legs in alcohol at —30°C. for thirty minutes, were heparinized intravenously for five or six days after exposure, the clotting time being kept between 30 and 60 minutes (Lee–White method). Eighteen of the animals escaped gangrene completely, whereas 3 showed some surface lesions without loss of the limb. Twenty control animals, exposed in the same way but not heparinized, lost their legs by complete gangrene, including the bone. These animals showed dry gangrene with spontaneous self-amputation (Fig. 4). Except for sterile dressings no surgical intervention was necessary in any of the animals. These findings, together with experience in 14 human patients with frostbite, treated before the introduction of heparin therapy, convinced us that an extremely conservative approach is indicated so far as amputations are concerned. Self-demarcation and the astounding recuperative power of frostbitten tissue force one to assume an attitude entirely different from that in cases of gangrene due to arteriosclerotic vascular disease.[14] Histologic examinations of the exposed

*We are indebted to Major Nathan B. Friedman at the Army Institute of Pathology, Washington, D. C., for permitting us to use the photomicrographs that resulted from our collaboration.

legs of the heparinized animals reveal that the red-cell conglomerates, regularly found in all smaller vessels of nonheparinized exposed animals, are missing.[12] The vessels are found empty or with a normal content of cells and plasma (Fig. 5). Since swelling and increased permeability, as evidenced by fluorescein tests, are observed to the same extent in heparinized as in untreated animals it must be assumed that the increased permeability leads to the accumulation of the red cells by stranding but that they cannot stick together if heparin is present in the blood stream.

A group of 8 volunteers who were undergoing treatment for subacute bacterial endocarditis at the Jewish Hospital of Brooklyn were put at our disposal through the kindness of Dr. Leo Loewe.[15] In 4 the frostbite was accomplished by means of a porcelain crucible filled with dry ice and applied without pressure to the skin of the lateral aspect of the upper arm for ten minutes. An area about 2 cm. in diameter came in contact with the skin, which attained a temperature of about —22°C. Heparinization was started immediately after exposure. One volunteer served as a control. The others were subjected to local refrigeration in the same manner but for two exposures of thirty minutes each. The initial or control exposure was permitted to develop for six days before the second frostbite was induced, immediately followed by subcutaneous injection of heparin in Pitkin menstruum.* The clotting time in the treated cases was kept between 25 and 60 minutes. All adequately treated lesions escaped deeper injuries, whereas the control subjects showed areas of central necrosis approximately 1 cm. in diameter and varying from 3 to 5 mm. in depth.

A second group, consisting of 4 volunteers (conscientious objectors†), was subjected to freezing of an area 3.5 cm. in diameter for thirty minutes by means of beakers filled with dry ice. Each volunteer received at least four exposures, including an untreated control, immediate heparinization for six days subsequent to exposure, heparinization for six days after an initial delay of twenty-four hours and heparinization for six days after an initial delay of twenty-four hours during which the exposed part was kept cool by means of an icebag applied to the lesion without pressure, to check on the validity of the concept that cooling subsequent to frostbite improves the course.[16]

The results were similar in all the volunteers. The untreated exposure led to gangrene. Immediate heparinization lasting six days prevented gangrene. Heparinization after a twenty-four-hour delay at room temperature gave almost as good a result as immediate heparinization. Cooling in the interim produced the poorest results (Fig. 6). Blister formation, which takes place rapidly in all exposed areas, is prevented in lesions kept cool after exposure. Immediately after the ice bag has been removed, however, the blisters arise rapidly and are even larger than those in the control lesions. This delay in the appearance of the blister may have led to the belief that cooling after exposure to low temperatures is beneficial.

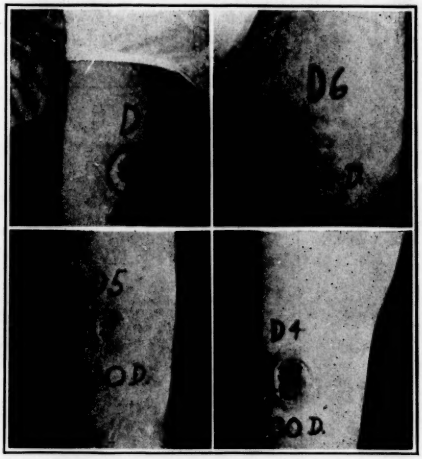

FIGURE 6. *Photographs of Skin Lesions on Leg, following Exposure to a Beaker Filled with Dry Ice.*

The two upper photographs, taken twenty-nine days after exposure, show two lesions in a volunteer; with the first (left) the subject received no treatment, and with the second (right) the subject was heparinized immediately and for six days after exposure. The lower ones, taken thirty days after exposure, show two other lesions in the same volunteer; with the first (left) the subject was heparinized, beginning twenty-four hours after exposure, for six days, and with the second (right) the subject was treated in the same way except that the area was cooled during the twenty-four hours after exposure.

The blister content in all heparinized patients stayed liquid throughout. No clot formation was noticed. If the blister did not rupture in the initial phase of marked tension its content was slowly resorbed, a loose shriveled piece of skin remaining on the exposed spot. The fact that heparinization keeps the interstitial fluid, with all its constituents, resorbable is of importance in the prevention of subsequent fibrosis and collagen replacement.

A third group of 3 volunteers (conscientious objectors) was subjected to freezing of an area 5 cm. in diameter by means of a metal capsule kept at —30°C. for thirty minutes. Each volunteer received at least five exposures that subsequently

*We have abandoned the use of heparin in Pitkin menstruum because of the great pain that accompanies the deposition. In animal experiments large hematomas were noted at the point of the second and subsequent injections that lead to exsanguination of the animals. In the animals, doses were used that were just sufficient to keep the clotting time for twenty-four hours between 30 and 60 minutes.

†Made available by Selective Service.

received, respectively, no treatment, warming for twenty-four hours after exposure but no heparinization, immediate heparinization for seven days subsequent to exposure, heparinization for seven days after an initial delay of twenty-four hours and heparinization for seven days after an initial delay of twenty-four hours during which the exposed part was warmed by an electric heating pad. The results were similar to those in the previous group. The untreated exposure led to gangrene, warming without heparinization made the gangrene more extensive, immediate heparinization prevented gangrene completely, and heparinization after twenty-four hours gave almost as good a result as immediate heparinization. Warming in the interval before heparinization produced a lesion that was almost as large as the untreated control lesion, although not so severe as the lesion with interval cooling in the previous group of volunteers. Although loss of tissue was completely prevented in the cases with early heparinization all sensation was lost for at least three months. The same loss of sensation occurred in the treated animals with complete maintenance of tissue. The motor disturbances in these animals, as demonstrated by dragging of the leg, disappeared in four to six weeks.

It was conspicuous in all the volunteers that the individual reaction to a standard exposure varied widely but was rather constant in the same subject. An exposure that consistently led to extensive gangrene of the entire exposed area in one volunteer failed to produce any tissue breakdown on repeated attempts in another. It may thus be possible to screen persons with an unusually high sensitivity to cold by means of standard test procedures.

The heparinization in the last two groups and in the following cases was carried out by intravenous drip. Approximately 300 mg. of heparin in 2000 cc. of physiologic saline solution per twenty-four hours was given at the rate of approximately 20 to 25 drops per minute. The clotting time (Lee–White method) was kept between 30 and 60 minutes and was checked every twelve hours. No untoward effects were seen in any of the cases treated by this method. Whenever possible, a vein on the middle part of the extensor surface of the forearm was used for the administration of the intravenous drip. The needle and a wide loop of the connecting tubing were fixed to the forearm by adhesive tape. No splint was used at any time, the patient thus being permitted to employ the

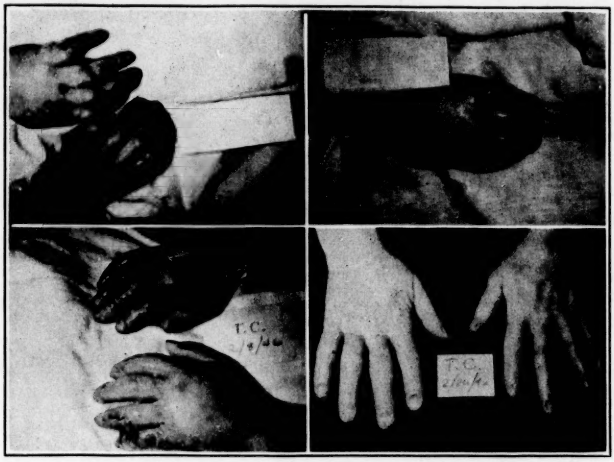

FIGURE 7. *Photographs of Hands That Were Exposed to a Temperature of 14 to 18°F. for Twelve Hours.*

The upper left photograph, taken six hours after exposure, shows edema and hemorrhagic blistering. The upper right, taken twenty-four hours after exposure, showed marked edema and large blisters. The lower left, taken four days after exposure and during heparinization, shows considerable edema but there was evidence of good circulation beneath the blisters. The lower right, taken three weeks after exposure, shows a complete return to normal, except for loss of the nails.

arm freely for eating and writing. The patient was even permitted to get off the bed while it was being made. In no case was it necessary to insert the needle more than twice.

Two actual cases of severe frostbite were treated by this method.[17] One patient had been exposed to a temperature of 12 to 13°F. for eight hours while lying with bare hands motionless on the pavement. The other had been exposed to a temperature between 14 and 18°F. while lying motionless with bare hands on the pavement for twelve hours. Both patients had severe degrees of hemorrhagic blistering within twenty-four hours of exposure. Heparinization was started six and ten hours respectively after the exposures and carried out according to the method mentioned above for seven and five days respectively. The hands were dressed under sterile conditions, since frostbitten tissues seem extremely susceptible to infection. Precautions similar to those employed in the treatment of burns were used, and wet penicillin dressings (1000 units per cubic centimeter) were applied to the blistered and denuded areas. Both patients escaped any loss of tissue except for the loss of the nails (Fig. 7). Although it cannot be stated with certainty that without treatment gangrene would have ensued, there is good reason to assume from previous experience that this would have occurred.

Summary

Gangrene subsequent to exposure to subzero temperatures in a dry surrounding (frostbite) was frequent in wartime and is by no means rare in civilian life.

The exposure to cold leads to a marked increase in capillary permeability that produces a rapid loss of plasma with stranding of the red cells in the capillaries. The red cells tend to stick together and to form occlusive masses, which finally undergo hyalinization.

If heparinization is begun within forty-eight hours of exposure and continued for seven to nine days the occlusive red-cell masses do not form, and subsequent gangrene is thus prevented as shown in animal experiments.

The plasma that leaks into the interstitial space and into blisters forms a dense fibrin deposit. Heparinization keeps this interstitial fluid liquid and resorbable. Cooling for twenty-four hours after the exposure increases the severity of the lesion.

Warming to 44°C. for twenty-four hours after exposure also increases the severity of the lesion. Room temperature seems to be best.

Heparinization of 15 human volunteers exposed to experimental frostbite revealed that gangrene can be prevented by this method. Damage to motor and sensory nerves, however, is not completely avoided.

Sensitivity to cold differs widely between different persons but is rather constant in the same subject. Exclusion of sensitive persons by spot freezing may thus be possible.

Two actual cases of severe exposure to cold that should have led to gangrene were treated by heparinization for five and seven days respectively. Both patients escaped any loss of tissue.

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ACUTE SUBPECTORAL ABSCESS: A SURGICAL EMERGENCY*

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BOSTON

CASE reports of acute subpectoral abscess and suppurative lymphadenitis — or "subpectoral phlegmon," as it is sometimes called — have appeared occasionally in both the American[1–3] and the foreign[4, 5] medical literature. The authors usually state that the condition is of relative infrequency, a contention seemingly borne out by a lack of any collected series. A review of the surgical records of the Massachusetts Memorial Hospitals for the past fifteen years reveals a group of 5 cases of acute subpectoral abscess or suppurative lymphadenitis, and 1 case is added from private practice.

Because the nature and behavior of this form of localized suppuration is unfamiliar to many physicians, it is apt to be treated expectantly and conservatively for relatively long periods. Surgery is usually resorted to after the process has spread widely, with extensive tissue destruction, and after a large abscess has broken into the axilla. Unfortunately, during this period the patient has had to endure a painful and toxic course of several days', or even weeks', duration. He may also have run the risk of extension of the suppuration into deeper and more vulnerable regions, such as the subscapular space, the pleural cavities, the mediastinum and the blood stream. Even when these serious complications do not develop he may experience prolonged disability from atrophy of disuse, as well as constricting scar tissue about the shoulder girdle. Surgical drainage is essential, since the sulfonamides and antibiotics cannot be relied on to control this type of infection. The very mechanism by which these agents ameliorate bacterial infection may delay liquefaction of the involved nodes and reduce the local inflammatory signs. As a result it may become more difficult to identify the site of the infection clinically, and the course prior to operative intervention and relief may be prolonged.

The essential pathology in this condition has been described in conjunction with several of the case reports referred to above. Bacteria of high virulence draining through lymphatic vessels from the primary focus, usually a relatively minor infection somewhere in the upper extremity, are filtered out by the infraclavicular lymph nodes. These nodes lie along the courses of the subclavian vessels lateral to the anterior scalenus muscle and the axillary vessels as far laterally as the axillary fascia and in the adjacent subpectoral adipose tissue. The infected nodes rapidly become swollen and edematous along with the surrounding fat and may proceed to necrosis and frank suppuration within a few days. Kanavel,[6] who presented an excellent description of the condition, called it a "subpectoral phlegmon." He considered it to be generally secondary to infection of the middle finger. Occasionally, the primary focus is on the chest wall or shoulder area or not even found. The infecting organism (as in 4 of the 6 cases presented below) is usually a streptococcus. Subpectoral infections due to other organisms, such as a staphylococcus (Case 6), are likely to result in a less fulminating pathologic process and a slower development of frank abscess. The infected mass of lymph nodes and the pus produced in association with it are enclosed in a fascial envelope whose lateral wall is formed by the tough axillary fascia. The relatively high pressure developed within this sac by the expanding inflammatory process provides a reasonable explanation for the great pain suffered by the patients. Edema and congestion of the overlying muscles and other soft tissues undoubtedly contribute to the general swelling of the region and to the symptoms. As the abscess enlarges, the axillary fascia may prove a more effective barrier to the suppuration than the less dense fascial planes beneath the scapula, along the vascular channels into the upper arm or toward the mediastinum. Pus may therefore dissect for considerable distances along these pathways before breaking out into the axilla.

The clinical syndrome in acute subpectoral abscess follows a fairly standard pattern. The patient develops pain in the shoulder and subpectoral area that is usually mild in the beginning but later is often exceedingly severe; there is also some malaise and fever. The shoulder becomes lame, and motion is limited and painful. When the infection is streptococcal the patient rapidly becomes extremely toxic, with a high temperature, chills, excruciating pain in the shoulder area and, in some cases, stupor or delirium. Infections due to other organisms, however, are less likely to manifest these more acutely toxic symptoms. Nearly from the beginning, there is a diffuse, although often only slight, swelling in the subpectoral region, the shoulder, the axilla and, to a lesser extent, the supraclavicular fossa; later, these areas may actually bulge. Tenderness may be marked. There is usually some local heat, redness and perhaps cutaneous edema. There

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may be a suggestion of deep induration, particularly beneath the pectoral muscles, but fluctuation usually cannot be elicited. This absence of fluctuation until a late stage of the disease, when a large abscess has broken out into the axilla, has two explanations. Initially, the pathology described above consists of a phlegmonous inflammation of the lymph nodes and surrounding fat; if the patient is seen at that time, of course, no fluctuation can be expected. Secondly, all the tissues involved are enclosed in the tough, resistant envelope of axillary and subpectoral fascia, deep beneath the pectoral muscles. Despite the presence of liquid pus here, fluctuation is difficult to demonstrate, therefore, until the suppuration has broken through the fascia into the subcutaneous fat of the axilla. This may require a week or more. A few small hyperplastic lymph nodes can be felt in the axilla or supraclavicular region but do not impress the examiner as being sufficient to explain the degree of fever and toxicity. The local findings in general suggest an acute inflammatory process in the region of the shoulder, and to those unfamiliar with the syndrome, the actual location of the infection may be puzzling and obscure. The shoulder joint and the neighboring bursas may be under suspicion, particularly since motion in the shoulder joint is limited and painful and the arm is held in some abduction.*

Early incision and drainage of the subpectoral and intraclavicular spaces provide the treatment for this type of infection and are indicated whether a frank abscess or only edematous masses of lymph nodes, with or without beginning suppuration, are encountered. Pain and toxic symptoms are relieved promptly in either case, and there is usually a dramatic fall in the temperature. Surgical drainage also permits bacteriologic studies and identification of organisms that may be susceptible to sulfonamides and antibiotics.

Most of the patients in this series were treated before modern antibacterial agents came into general use. In only 1 case was an agent theoretically specific for the causative bacteria administered in adequate dosage. Since the symptoms and signs failed to improve after more than forty-eight hours of intensive treatment with penicillin preoperatively but responded dramatically to simple incision and drainage of the subpectoral space, it is almost certain that the process would not have resolved under the medical therapy alone. Little actual pus was encountered in this particular case, the chief finding being a mass of swollen and edematous lymph nodes and fat, culture of which revealed a hemolytic streptococcus. Sulfonamides and antibiotics are probably helpful in limiting the spread of the infection and should therefore be employed in all cases as adjuncts to the surgical treatment.

The technic of surgical drainage is simple. Direct access to a subpectoral abscess may be obtained by incision of the axillary fascia along its junction with the lateral margin of the pectoralis major muscle followed by breaking through of the abscess wall by blunt dissection. If only a mass of infected lymph nodes is encountered, the forefinger may be used to dissect bluntly well up into the space along the axillary vessels as high as the anterior scalenus muscle. A slightly curved skin incision made at right angles to the anterior axillary fold rather than parallel to it should reduce the postoperative scar disability, an important consideration. When necessary, counterincisions are made to gain good dependent drainage, and several Penrose drains are inserted.

Case Reports

Case 1. C. M., a 54-year-old man, was admitted to the Burbank Hospital, Fitchburg, Massachusetts, on July 14, 1939. Four days previously mild chills and fever, with pain and stiffness at the base of the neck on the left, had developed. These symptoms were interpreted initially as being due to influenza. On the following day the pain became worse, the patient had a high temperature, and a swelling appeared in the left pectoral region.

When the patient was seen by one of us (T. J. A.) in consultation on the day after admission the temperature was 102°F., and he appeared extremely toxic and had some difficulty in breathing. The left pectoral region was involved in a massive, tense swelling extending from the clavicle down over the midportion of the chest and also into the axilla. The overlying skin was cyanotic and showed dilated veins but was not erythematous. The whole area was surprisingly nontender. Aspiration of the region of maximum swelling yielded pus, confirming the diagnosis of subpectoral abscess.

Incision and drainage were then performed immediately under oxygen and ether anesthesia, the primary incision being placed over the site from which pus had been obtained and extending parallel to the direction of the pectoralis muscle fibers. These fibers were split, giving access to a large abscess cavity extending above almost to the clavicle, medial to the sternum and bulging laterally into the axilla. A large amount of thick, yellow pus gushed out. Drains were inserted through counterincisions made in the anterior axilla and on the chest wall into the most dependent parts of the cavity. Bacteriologic studies of the pus showed streptococci.

The patient's general condition improved dramatically, and the temperature dropped gradually, being entirely normal on the 12th postoperative day. There was a short exacerbation of the fever 3 days later, when a hemorrhage followed the removal of a drain and the wound had to be packed. Two or three 1-gm. doses of sulfanilamide, but no other chemotherapy, were given at that time.

Postoperatively, the patient stated that 7 or 8 days before admission he had accidentally burned the tip of a finger of the left hand. The resulting blister was cut away, and the finger dressed at the shop dispensary. Subsequently, the finger became somewhat tender and painful prior to the development of the acute symptoms described above.

This typical case of acute subpectoral abscess was recognized as a surgical condition before serious extension of the process had occurred. It responded well to adequate incision and drainage without the benefit of chemotherapy.

Case 2. M. D., a 9-year-old schoolgirl, was admitted to the hospital on August 6, 1935. Three weeks previously she

*Cases of similar infections involving the retroperitoneal iliac lymph nodes, secondary to a primary focus in a lower extremity, have been observed. The responsible organisms in these cases are usually streptococci, and dramatic improvement follows surgical drainage of the retroperitoneal space.[1]

had sustained a laceration in the region of the right elbow in a fall. After treatment at home the wound appeared to be healing, but 1 week later, after the child had picked off the scab, the arm became swollen, and she complained of pain in the axilla and developed fever and malaise. She was

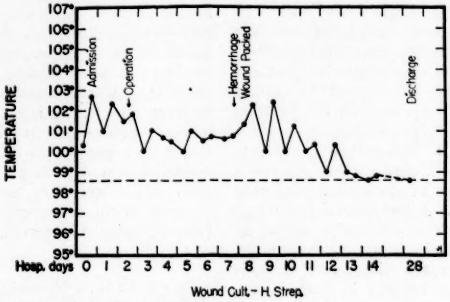

FIGURE 1. *Case 1.*

treated for 1 week or more at home with hot poultices to the axilla, without improvement.

On admission the child appeared sallow and moderately dehydrated. The right arm was held in a position of partial abduction, and shoulder motions were limited in all directions because of the muscle spasm and pain. The right axillary region was tender. Enlarged axillary lymph nodes could be felt, but there was no fluctuation, redness or real

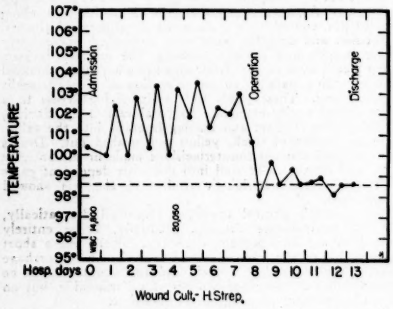

FIGURE 2. *Case 2.*

bulging. A recently healed skin scar was noted over the right olecranon process. The remainder of the physical examination was negative.

The temperature was 100.6°F., the pulse 90, and the respirations 20.

Examination of the blood disclosed a white-cell count of 14,800, with 67 per cent neutrophils. Other laboratory studies were not remarkable. X-ray examination showed a normal chest and no lesion in the bones of the right shoulder girdle.

After 4 days of expectant treatment, swelling of the right pectoral region was apparent, and the right axilla became tenser and extremely tender, but never fluctuant. The temperature continued in its septic course, rising at times to 103°F. The white-cell count at that time was 20,050, with 76 per cent neutrophils. When definite fluctuation was demonstrated in the axilla 2 days later, a subpectoral abscess containing over 75 cc. of thin, yellowish pus was drained surgically, and a pack inserted. Culture of this pus showed a pure strain of hemolytic streptococcus. The temperature fell to normal within a few hours of the drainage, and the patient made a rapid recovery.

Early recognition of the true lesion in this case would have saved the patient over two weeks of pain and disability.

CASE 3. H. M. P., a 28-year-old medical student, was admitted to the hospital on January 23, 1935. Two weeks previously the patient had accidentally pricked the middle finger of the left hand while doing an autopsy. This seemed to heal within a few days, and he was apparently well until 2 days before admission when a pain suddenly developed in the left arm near the shoulder during lifting and became quite severe. During the evening he began to have chills and fever and general malaise. The pain progressed, involving all the left shoulder and the side of the neck. Attempted motion of the shoulder and the left arm was extremely painful.

Physical examination revealed an extremely uncomfortable and moderately toxic patient. The left axillary region seemed slightly swollen and quite tender, and a few small lymph nodes could be felt. The left shoulder anteriorly and the clavicular and pectoral regions were tender to touch. There was only slight swelling in the upper arm and no lymphangitis. A 1-cm. healed scar was seen on the dorsum of the left middle finger, with slight redness at its margins. In the absence of actual fluctuation in the axillary region, the attending physicians did not consider surgery to be indicated. The patient continued to experience a great deal of pain in the involved areas and to have fever and chills.

The temperature was 102°F., the pulse 100, and the respirations 25.

A blood culture showed no growth. X-ray films of the shoulder joint and the bones of the shoulder girdle were negative for signs of infection.

On the supposition that this was an acute rheumatic arthritis a course of salicylates was given. The swelling over the anterior aspect of the shoulder and pectoral region increased, and the skin became generally tenderer to touch, but still fluctuation was absent. The fever continued in its septic course with gradual subsidence to almost normal 10 days after admission. The white-cell count rose, however, to 26,350, with 79 per cent neutrophils on January 28. The pain and the local signs continued, and on February 5, when fluctuation finally became apparent in the anterior axilla, the area was incised with the drainage of 30 cc. or

more of thick, white pus, a culture of which showed hemolytic streptococcus and *Staphylococcus albus*. The fever flared up again; the pain continued, particularly in the upper arm, and the white-cell count rose to 34,000. On February 14 surgical drainage of an abscess on the posterior aspect of the left forearm released a great deal of pus. This abscess was found to connect with the original subpectoral abscess cavity. Culture of the forearm cavity showed hemolytic streptococci. The temperature finally reached normal on February 22 as the infected wounds gradually cleared up. Shoulder function returned completely in time, but the patient noticed a numbness of ulnar-nerve distribution in the left hand for over 1 year.

Delay in surgical drainage of the subpectoral abscess in this case resulted in local spread of the suppurative process, eventually requiring multiple incisions and a prolonged recovery period. Surgery was deferred until actual fluctuation appeared.

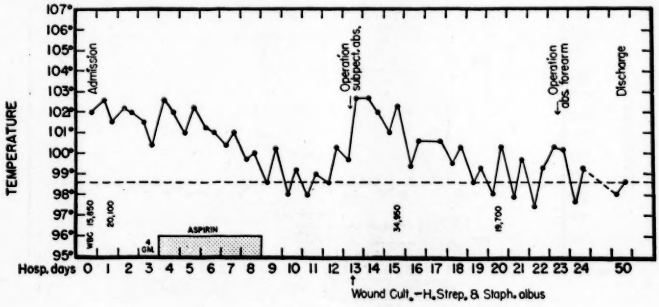

FIGURE 3. *Case 3.*

CASE 4. G. C., a 17-year-old boy, was admitted to the hospital on January 30, 1946. Three days previously the patient had accidentally scraped some skin from the knuckle of the right middle finger. On the following day he was able to squeeze a little pus from the wound, and that night developed malaise, insomnia and a mild chill, with fever. He gradually became sicker, and on the day before admission the temperature rose to 104.5°F. He vomited and was anorexic. On the morning of admission he was so groggy and toxic and the neck muscles were so stiff and sore that he was thought by his physician to have meningitis and was admitted to the Contagious Department of the Massachusetts Memorial Hospitals.

Physical examination showed considerable pain in the right shoulder region, and the patient appeared quite drowsy. There was moderate swelling over the pectoral region, with tenderness on deep palpation. The right arm was held in slight abduction, and motion in general, particularly further abduction, was painful. There was some stiffness of the neck muscles, particularly on the right side. There was a recently healed abrasion of the skin on the dorsum of the right middle finger. The remainder of the examination was essentially negative. A lumbar puncture revealed normal fluid.

The temperature was 101.6°F., and the pulse 124.

Examination of the blood disclosed a white-cell count of 13,050, with 90 per cent neutrophils. The urine gave a ++++ test for ketone bodies but was otherwise normal. The temperature rose gradually to 105°F. within 36 hours, and the white-cell count to 15,700, with 91 per cent neutrophils. The swelling of the right pectoral region also increased. Some swelling appeared in the axilla and spread to the right shoulder and supraclavicular regions. The patient was then given 25,000 units of penicillin every 3 hours intramuscularly. The temperature, however, continued between 103 and 104°F., and there was no improvement otherwise. The question of pneumonia was raised, but x-ray examination of the chest was negative.

When seen in surgical consultation by one of us (K. B. L.) 2 days after admission the patient was thought to have an acute suppurative lymphadenitis or possibly actual abscess formation in the subpectoral region, and was therefore transferred to the main hospital on the afternoon of February 1, for incision and drainage. As a further trial of conservative therapy, the penicillin was continued overnight in doses of 50,000 units intramuscularly every 3 hours. On the following morning, although the temperature had dropped slightly to 103°F., the pulse was still 124. The patient not only felt unimproved but also complained of increased pain, with some pain extending into the left upper chest wall and over the clavicle. Edema had spread slightly to this, which was tender to touch.

In view of the lack of improvement after 60 hours of intramuscular penicillin and for fear that the infection was about to penetrate into the mediastinum, incision and drainage of the right subpectoral space were done under endotracheal nitrous oxide and ether anesthesia. A mass of edematous lymph nodes and fat was found filling this space up along the axillary vascular sheath, and several cubic centimeters of thin pus was liberated. Cigarette drains were inserted. Cultures of the pus revealed a mixed growth of hemolytic streptococcus, a streptococcus with alpha hemolysis and a weakly pigmented hemolytic *Staph. aureus*.

Postoperatively, the penicillin was continued in the same dosage every 3 hours, and sulfadiazine was given in full dosage by mouth, so that a blood level of 8 to 10 mg. per 100 cc. was maintained. The temperature fell dramatically to 100°F. within 2 hours of operation and then gradually subsided to normal on the 2nd postoperative day. The clinical symptoms improved nearly as rapidly, and the patient was discharged feeling fine, with a nearly normally functioning shoulder and only a slightly draining wound, on the 7th postoperative day. The white-cell count at that time was 9000. Within 2 days, however, the shoulder pain recurred, and the patient was readmitted 4 days after discharge with a temperature of 102°F., some toxicity and considerable swelling in the right supraclavicular fossa. The white-cell count at that time was 15,400, with 81 per cent neutrophils. This was considered to represent a flare-up of the infection in the supraclavicular lymph-node group, and not in the subpectoral space. The incision into the sub-

pectoral space was dry and nearly healed, and probing released only a tiny amount of clear serum. The temperature dropped to normal in less than 48 hours on combined treatment with 20,000 units of penicillin every 3 hours and 1 gm. of sulfadiazine every 4 hours. As a safeguard, these drugs were continued for another week, the patient then being discharged cured.

This case represented fulminating suppurative axillary lymphadenitis relieved promptly by early recognition and surgical drainage. Despite intensive administration of penicillin, surgical drainage was necessary to control the principal focus of infection.

CASE 5. R. S., a 22-year-old man, was admitted to the hospital on March 17, 1941. Two days previously he had first noticed pain and swelling of the right shoulder region and upper arm but had felt well otherwise. On the day before admission the swelling extended to the pectoral region, and motion of the shoulder became painful. That evening he had fever without chills. There was no history of trauma or of antecedent infection of any sort.

On physical examination the patient appeared slightly toxic and rather uncomfortable. There was a pronounced swelling, without erythema or edema of the skin, over the entire right pectoral area and to a lesser extent in the axilla and over the region of the anterior shoulder and lower neck. The arm was held at about 20° of abduction, and such movement was painful. Two slightly enlarged tender lymph nodes were felt in the lateral axilla (brachial nodes).

The temperature was 102°F. and the pulse 96.

Examination of the blood disclosed a white-cell count of 13,000, with 79 per cent neutrophils. The blood chemical findings and other laboratory studies were normal. X-ray examination of the shoulder girdle showed no evidence of diseased bones or joints. A diagnosis of acute subpectoral abscess or suppurative lymphadenitis was made within a few hours of admission.

Incision was promptly performed by one of us (K. B. L.), revealing an acute edematous mass of lymph nodes in the subpectoral space. This space was thoroughly opened up by incision both through the axilla and down through the subpectoral muscles over the point of maximum swelling. Bacteriologic examination of material from the wound showed a pure culture of *Bacillus subtilis*. The pain was promptly relieved by this procedure. The temperature fell gradually to normal in 48 hours, without a definite purulent discharge at any time. The temperature then rose again to 100°F., where it remained for 5 days. This was thought to be due to a thrombophlebitis of the right axillary and brachial veins that had become apparent at that time. Swelling and soreness of the arm and shoulder subsided with elevation of the arm and moist heat treatment. The patient was discharged on the 16th postoperative day, with only minimal residual disability of the shoulder and arm.

In this case an acute subpectoral lymphadenitis, apparently due to an organism of low virulence, was encountered. No primary focus was found.

CASE 6. A. M., a 19-year-old boy, was admitted to the hospital on July 31, 1933. The patient had first noted pain in the right axilla 11 days previously, followed by swelling throughout the upper arm, the shoulder region and the axilla. The pain then became excruciating, particularly on motion of the shoulder. The patient became anorexic, somewhat toxic and feverish. Three weeks before admission and 10 days before onset of the symptoms, he had noted a small furuncle just to the right of the sternum, which he had squeezed several times, but later this had seemed to heal.

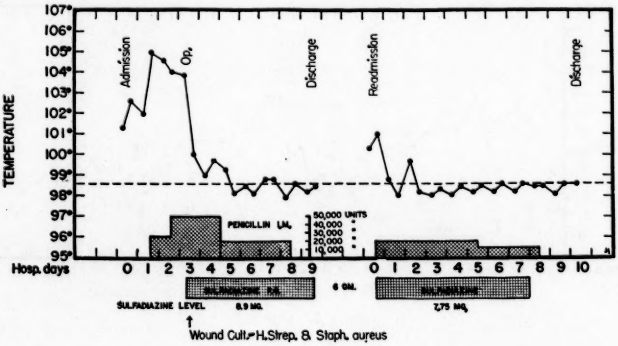

FIGURE 4. *Case 4.*

Physical examination revealed a small, nearly healed furuncle near the sternum. A large, tender, moderately reddened swelling was noted in the region of the right pectoralis major muscles.

The temperature was 100.6°F.

Examination of the blood disclosed a white-cell count of 13,300, with 83 per cent neutrophils. The urine showed a slight trace of albumin, and the sediment contained rare white cells and a few red cells. X-ray examination of the lung fields was negative.

On the following day a large right subpectoral abscess was incised and drained through the axillary route. A large mass of blood clots with some inflammatory tissue and definite pus was found in the space. This was cleaned out, and a gauze pack was inserted. A culture of the fluid revealed a hemolytic *Staph. aureus*. On the evening of the day of operation the temperature was 99°F. and thereafter was normal. The patient was discharged on the 7th postoperative day, having made a good recovery.

The infection in this case, which was due to a staphylococcus, was definitely less acute and severe than the streptococcal infections described above. Incision and drainage of the abscess resulted in prompt relief, although the patient could have

been saved a week or more of pain and invalidism by an earlier diagnosis.

Summary

A series of 6 cases of acute subpectoral abscess or suppurative lymphadenitis, usually secondary to minor infections in the upper extremity, is reported. This infection is more toxic when due to streptococci than when due to staphylococci or other organisms.

Demonstrable fluctuation is regarded as a late and uncertain manifestation of this syndrome, presumably because the involved lymph nodes may be slow to suppurate and because the abscess when formed is enclosed in a tough fascial envelope deep beneath the pectoral muscles.

Early incision and drainage, which provide the treatment of choice, prevent the extension of the suppurative process to other regions and bring about rapid subsidence of the infection and almost immediate relief of pain.

Sulfonamide and antibiotic therapy is a valuable adjunct to surgery in this condition, but cannot be relied on to control the infection alone.

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ECZEMA VACCINATUM

Report of a Case

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BOSTON

UNTOWARD reactions following vaccination are rare. The clinical entity known as eczema vaccinatum, a type of generalized vaccinia, is one such complication. According to estimates, generalized vaccinia occurs in the ratio of 1 case to 20,000 or 40,000 vaccinations.[1] Because of its rarity, the diagnosis may not be readily apparent. Occasionally, the admission of a patient with unrecognized eczema vaccinatum to the skin ward of a hospital results in an outbreak among those exposed.[2]

Generalized vaccinia is the term applied to the generalized eruption of typical vaccinial lesions that occur after vaccination. It varies in degree from a mild illness with a few scattered lesions to a severe fatal infection and a clinical course similar to that of smallpox. Eczema vaccinatum occurs for the most part in children with chronic skin disease who have been exposed to cow-pox virus either by vaccination or by contact with a vaccinated person.

It is the purpose of this discussion to present the clinical and laboratory findings in a recent case of eczema vaccinatum. The clinical diagnosis was confirmed by a positive Paul test. Treatment with penicillin, which had been instituted before the illness had been diagnosed, was continued, the purpose being to minimize the possible effects of secondary invaders.

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S. H., a 2-year-old boy, was admitted to the hospital on May 3, 1946, because of an exacerbation of a cutaneous eruption that had been present for about 6 weeks. The family physician, who was treating the child for eczema of the flexor surface of both elbows and knees, reported that tiny, pearl-like lesions had appeared at the periphery of the eczematous areas 4 days before admission. Two days later the lesions had spread over the entire areas previously involved in the eczema. The mother noted flushing of the face, and the child appeared quite ill. An older sibling had been vaccinated 13 days before unusual signs and symptoms had been noticed in this patient.

Physical examination revealed a well nourished child who did not appear to be extremely toxic. There was generalized lymphadenopathy. Over the skin of both antecubital and popliteal areas, individual lesions had coalesced into a grayish purulent mass (Fig. 1 and 2). At the periphery the pustules were discrete and extended over both arms to the wrists. A few discrete umbilicated pustules were present over the face and lids and in the hair. Physical examination was otherwise negative.

The temperature was 103.4°F., the pulse 110, and the respirations 24.

The red-cell counts on May 4 and 7 were 3,200,000 and 3,540,000 respectively, and the hemoglobin determinations on the same days were 10.2 and 12.1 gm. The white counts from May 3 to May 7 varied from 12,500 to 22,400. A smear on May 7 showed 62 per cent neutrophils, 30 per cent lymphocytes, 1 per cent monocytes and 7 per cent eosinophils. A urinalysis on May 4 was negative. A sulfadiazine level of 6.8 mg. per 100 cc. was reported on May 7. A culture from a draining lesion revealed a nonhemolytic *Staphylococcus aureus*.

Scarification† of the cornea of a rabbit with scrapings of lesions taken on May 6 revealed Guarnieri bodies in epithelial cells scraped from the eye 3 days after inoculation (Fig. 3).

The temperature rose to 105.4°F. on the day of admission and fluctuated between 100 and 105°F. until May 9. On May 7 several new pustules appeared on the face, legs and

†The Paul test was performed by Dr. Frederic Parker, Jr., pathologist-in-chief, Mallory Institute of Pathology, Boston City Hospital.

trunk. On the following day there was a moderate amount of purulent drainage from the lesions in the popliteal and antecubital areas. During that time the patient had become irritable and restless, crying out frequently. As the pustules dried and scabs formed, the drainage changed from a purulent to a serous exudate and gradually disappeared.

Treatment with penicillin and sulfadiazine was started on admission. Penicillin was administered in a dosage of 10,000 units every 4 hours until May 12, and sulfadiazine in a dosage of 0.5 gm. every 4 hours. Chemotherapy was halted on May 7, when a morbilliform eruption appeared on the face and anterior and posterior aspects of the chest. The temperature fell to 98.9°F. on May 10 and except for a rise to 102°F. on May 12, remained normal thereafter. Recovery was uneventful. No scars were noted at an examination several months later.

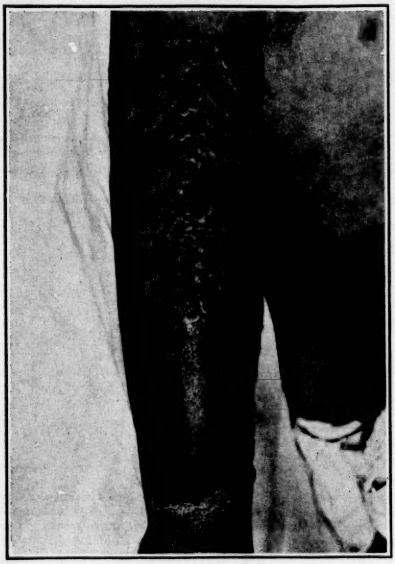

FIGURE 1. *Vaccinial Lesions in the Antecubital Space of the Right Arm.*

FIGURE 2. *Vaccinial Lesions in the Popliteal Spaces.*

Although this patient had not slept in the same bed with the vaccinated child, no attempt at segregation had been made, and there was ample opportunity for direct contact between the children. In addition to direct contact, however, infection of the skin of the eczematous patient by droplet infection must also be borne in mind. In 1929 vaccine virus was demonstrated in the upper respiratory tract four or five days after vaccination.[3] Increased susceptibility of patients with skin disease to vaccine virus is well known. In the case reported above the patient himself had not been vaccinated.

Heightened susceptibility of eczematous children has also been noted to Kaposi's varicelliform eruption. Since the first description of this skin disease by Kaposi[4] there has been a great deal of disagreement concerning its causation and relation to eczema vaccinatum. When there has been no history of vaccination or of contact with a recently vaccinated person, the diagnosis of Kaposi's vari-

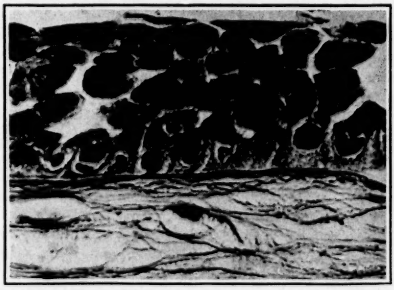

FIGURE 3. *Photomicrograph Showing Guarnieri Bodies in the Epithelial Cells of the Rabbit's Cornea.*

celliform eruption is usually made. The isolation of herpes virus from patients ill with the latter infection[5–7] has differentiated it from eczema vaccinatum, which is of course due to the vaccine virus.

Outbreaks of both eczema vaccinatum and Kaposi's varicelliform eruption have occurred on skin wards following the admission of patients suffering from this infection. Danziger[2] reported such an outbreak on the open ward of an infants' hospital in which 5 out of 6 children with skin disorders contracted vaccinia after the introduction of a patient with generalized vaccinia. McLachlan and Gillespie[8] described an outbreak of Kaposi's varicelliform eruption in which 16 cases occurred in a dermatologic ward under similar circumstances.

Chemotherapy has been employed in the treatment of both infections for its possible effect on secondary invaders. For the same reason penicillin was used in the treatment of the patient described above.

A case fatality rate of 33 per cent has been reported for eczema vaccinatum.[9] Although the clinical course is mild in some cases, patients whose illness is complicated by secondary pneumonia or severe skin infection may be quite ill. It is possible that penicillin has considerable influence in reducing the high case fatality rates associated with eczema vaccinatum.

One or two simple precautions concerning vaccinations must be re-emphasized. Vaccination should be deferred on patients with skin disorders until recovery has occurred. Vaccinated persons should not be allowed to be exposed to patients suffering from skin infections. If these simple rules are observed the exceedingly low incidence of generalized vaccinia will be reduced to an even greater extent.

Summary

A case of eczema vaccinatum is presented in which the infection occurred as a result of contact with a vaccinated sibling. The clinical diagnosis was confirmed by a positive Paul test.

Precautionary measures, such as deferring vaccination of patients with skin disorders and preventing exposure of such patients to vaccinated persons, will reduce to an even greater extent the present low incidence of generalized vaccinia.

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SUBPHRENIC ABSCESS FOLLOWING PRIMARY CLOSURE FOR PILONIDAL SINUS*

Report of a Case

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THE problem of the proper management of pilonidal sinus has occupied a position of increasing importance in the medical literature in the past six years. In the medical care of an active military force of several million generally healthy men and women, pilonidal cyst and sinus have been among the most frequent surgical causes of disability. It is the purpose of this communication to indicate some of the hazards attendant on the primary closure of pilonidal wounds.

Before the war the surgical procedure in widest usage was radical excision, a granulating wound being left to heal by secondary intention. Primary closure of a pilonidal wound had been advocated by some but in general had been given up because of a disturbing number of recurrences (or so-called "persistences") and an occasional severe infection in the sutured wound. Contributing to these complications were the tendency to limit the extent of the excision to preserve tissue for the closure; technical difficulties in obliterating the dead space; the location of the operative field in a region prone to perspire freely and in proximity to the rectum and anus; and perhaps a failure adequately to evaluate the extent of inflammatory changes present at the time of operation.

With the advent of chemotherapy — first, the sulfonamides, followed by penicillin and more recently by streptomycin — there occurred renewed interest in attempts at primary suture of the pilonidal wound. This approach received a tremendous impetus during the war years, when it was considered important to eliminate the loss of time necessary for the healing of a granulating wound. The objective of returning a man to active duty as soon as possible led to a policy of primary closure in a large proportion of cases in almost every service hospital. The ready availability of the chemotherapeutic agents for the control of infection lent courage to these efforts.

That no single method of primary suture has been pre-eminently successful is evidenced by the great number and variety of procedures devised to meet the problem. One of the most promising technics for obliterating the dead space is that of utilizing gluteal muscle — fascial flaps, as described by Pope[1] and further reported by Holman.[2] The latter advocates avoiding skin-penetrating sutures and completes the closure with a subcuticular stitch of wire or dermol. The use of silk is recommended by Dunphy and Matson.[3] Cotton has been employed by Ziegler et al.[4] and Larkin[5] finds stainless steel the material of choice. All these authors stress the value of meticulous operative technic and care in the postoperative management in lowering the recurrence rate, whether primary closure has been performed or the wound permitted to heal by granulation. There is general agreement that only about 60 per cent of cases are suitable for primary closure and that the recurrence rate with primary closure is slightly higher than that with the more tedious granulating process. Burns,[6] in a study of civilian cases, reports some success with various methods of closure but finds that the most generally effective results have been obtained by permitting the wounds to granulate. It is difficult to evaluate the end results among service personnel because of the limitations imposed by military conditions on an adequate follow-up study.

The emphasis on primary closure and the protection afforded by chemotherapy have tended to minimize the potential risk entailed in this procedure. The following case, in which a fatal result from overwhelming infection was averted by a narrow margin, is an example in point. The multiple operations were performed by various members of the surgical service of a large naval hospital.

W. R., a 17-year-old seaman, entered the hospital on March 5, 1945, because of a small draining sinus in the intergluteal cleft, with a narrow surrounding area of induration. Under treatment with Sitz baths the inflammatory reaction subsided rapidly, and drainage from the sinus ceased. Ten days after admission, under procaine spinal anesthesia, the cyst was excised en bloc, together with an ellipse of overlying skin. The cyst extended to the lower end of the coccyx and penetrated the coccygeal bone for a short distance. The fascia was closed with interrupted sutures of chromic catgut. Skin closure was performed with figure-of-8 sutures of No. 32 steel wire, and the wound was not drained.

Two days after operation the temperature rose to 102°F., associated with wound pain and tenderness. The sutures were removed, and the infected wound was packed widely open. During the next 4 days discharge from the wound became profuse and foul-smelling; the temperature rose to 104°F., associated with a pain in the right posterior portion of the chest. On the 5th postoperative day there was marked peripheral collapse and delirium; the pulse was 138, the respirations 55, and the blood pressure 80/60. The chest pain continued, but there was no cough or expectoration, and there were no abnormal physical signs referable to the thorax. The abdomen was rigid, and there was no pain, tenderness or vomiting; flatus and loose stools were passed. There was no pain or tenderness of the extremities. The white-cell count was 13,800, with 71 per cent neutrophils and 12 per cent band forms; the hemoglobin was 13.5 gm. A roentgenogram of the chest showed clouding of the right lower-lung field.

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The patient ran a septic course, with swinging temperatures to 106°F. and marked rapid deterioration in his general condition. At no time were shaking chills noted, and blood cultures were consistently negative for both aerobic and anaerobic organisms. Intensive supportive therapy included maintenance of fluid and electrolyte balance by means of parenteral fluids containing glucose, salt, vitamins, calcium, plasma and Amigen, fourteen transfusions of whole blood and oxygen. Chemotherapy consisted of 20,000 units of penicillin every 2 hours intramuscularly, supplemented by 40,000 units of penicillin and 6 gm. of sodium sulfadiazine by the intravenous route daily. The total amount of penicillin given was 8,100,000 units, and that of sulfadiazine 120 gm.

It was the clinical impression that a retroperitoneal cellulitis accounted for the extreme toxicity and abdominal rigidity. An indurated area in the right infrascapular region was incised on April 5, and necrotic foul-smelling tissue was encountered. On April 28 there was a sudden profuse drainage of foul-smelling greenish-yellow pus from this wound. Roentgenograms showed pooling of lipiodol in the right subphrenic space. Fluoroscopy demonstrated that the right leaf of the diaphragm was elevated and fixed; a diffuse haze occupied the right lower-lung field.

The diagnosis of a large right subphrenic abscess was then established. Expectoration of foul-smelling material similar to that on the dressings indicated a bronchopleural fistula. On May 2 an incision was made in the right midaxillary line over the ninth interspace. The pleura was pushed aside, the fibers of the diaphragm were separated with a clamp, and a large quantity of foul-smelling yellow-grey pus was evacuated; this was positive on culture for *Escherichia coli*, *Streptococcus faecalis* and *Staphylococcus aureus*. Copious amounts of pus drained from this site for 2 weeks, and the temperature elevations fell to between 102 and 103°F. The expectoration of purulent material promptly ceased and did not recur. On July 27 a thoracotomy and rib resection were performed, a chronic empyema sinus being unroofed. After this procedure the patient became afebrile, and there was rapid and steady improvement. By November 15 all the wounds had healed, and the weight had risen to 158 pounds from a low of 104 pounds. The pilonidal wound had been completely epithelialized within 3 months of the original operation. The patient was discharged from the hospital 1 year after an operation generally classified in the "minor" category. A follow-up letter 10 months later disclosed that he was experiencing no restriction of his activities; there had been no recurrence of the pilonidal cyst.

It is apparent that any operative procedure that possibly entails the sequelae experienced in the case presented above is not to be considered lightly. It may be contended that this case was not suitable for primary closure; yet the inflammation present on admission was only moderate in degree and subsided rapidly before the operation was undertaken. The objections that chemotherapy should have been instituted before operation and that larger doses should subsequently have been exhibited may be valid. The combination of *Esch. coli*, *Str. faecalis* and *Staph. aureus*, however, is one against which it would be difficult to issue a guarantee of protection with the means currently available. Contamination of the wound presumably occurred as the result of injury to the rectum, either during the process of mobilization of the cyst or in the placing of the deeper sutures. Such an accident may easily pass unnoticed.

Sweeping conclusions regarding the merit of a surgical procedure would certainly be hazardous on the basis of a single accident such as this. Careful selection of cases, meticulous operative technic and the judicious exhibition of chemotherapeutic agents may all contribute to the elimination of a large part of the risk incurred when primary closure of a pilonidal wound has been performed. It is suggested, however, that packing the wound widely open and permitting healing by granulation be considered the method of choice in the hands of the inexperienced operator or when there is any evidence of recent inflammation in the local lesion.

Summary

A case of pilonidal sinus treated by excision and primary closure is presented.

The postoperative course was characterized by a fulminating retroperitoneal cellulitis, right subphrenic abscess, bronchopleural fistula and empyema. Although recovery was ultimately effected, a fatal issue was narrowly averted.

It is suggested that the primary closure of pilonidal wounds be reserved for cases conforming to limited criteria. In the hands of the less experienced surgeon, or in the presence of recent inflammation, the procedure of total excision, packing the wound widely open and permitting healing by granulation may be indicated.

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MEDICAL PROGRESS

CHEMICAL FACTORS IN ASTHMA (Concluded)*

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BOSTON

BLOOD SUGAR

Numerous investigators have thought that there might be a disturbance in the metabolism of sugar in patients suffering from asthma and allergic conditions. In 1924 Ramirez, St. George and Moses[43] examined the levels of the blood sugar in 40 patients, 28 of whom had asthma and hay fever. Determinations were made before and after treatment, but they revealed no uniform differences in the levels of the blood sugar at these two periods.

In 1929 Malone[44] found the average fasting level of blood sugar to be 75.4 mg. per 100 cc. in 15 patients with allergic asthma associated with food sensitivity. In 1933 Black[45] reported an average fasting blood sugar level of 78.9 mg. per 100 cc. in 100 patients who had a definite history of allergy, and he concluded that more than half the patients with hay fever and asthma have fasting blood sugar values below the normal range and that the sugar tolerance is definitely elevated.

In 1936 MacQuiddy, McIntyre and Koser[46] published their findings of fasting blood sugar levels and tolerance curves on 20 patients with asthma and hay fever and 21 normal subjects used as controls. They found no significant difference between the two groups. In 1937 Wagner and Rackemann[47] studied the blood sugar in 24 patients with asthma and hay fever, using both venous and capillary bloods. In all cases the fasting blood sugar and the glucose-tolerance curves were essentially normal.

In 1939 Waldbott, Ascher and Rosenzweig[48] attempted to make a more crucial study. They selected a group of 14 patients sensitive to pollen who were given a slight overdose of pollen extract. During the mild general reaction that supervened, the blood sugar was determined at intervals of fifteen minutes. The values showed an immediate transient rise followed by a prolonged fall to an average level of 63 mg. per 100 cc., which took over two hours to return to the basic level. When the same procedure was carried out on 24 patients who did not develop any reaction to the pollen dose, the blood sugar remained steady. Also, in 22 nonallergic persons who were given pollen injections corresponding to the amounts received by the allergic group, the blood sugar did not change.

In 1939 Joseph[49] had a different concept. He treated 104 patients, of whom 96 had asthma and 34 had arthritis or arthrosis, with eight to twelve daily injections of 8 units of insulin, and he claimed that the patients improved.

In 1941 Abrahamson[50] suggested a reciprocal relation between asthma and diabetes. Asthmatic patients were made worse by sodium chloride, and diabetic patients better; the former were prone to hypothyroidism, and were relieved if they developed hyperthyroidism, the reverse being true for the latter. The two diseases, although frequently occurring among members of the same family, were mutually exclusive and were rarely observed in the same person at the same time. Asthmatic attacks occurred with a tendency to hypoglycemia, and drugs relieving asthma raised the level of the blood sugar. The author assumed that bronchial asthma was associated with hyperinsulinism, and the glucose-tolerance curves of 12 patients with asthma corresponded to those found in cases of hyperinsulinism. The patients improved on a high-fat, low-carbohydrate diet, and this fact was supposed to justify the claim that hyperinsulinism was one of the conditions necessary for the appearance of asthmatic attacks. It was a logical explanation for the frequency of nocturnal asthmatic attacks when the blood sugar level was low, and it explained the failure of glucose to effect a lasting remission. Vollmer,[51] on the other hand, in 1939, had treated 7 children with severe asthma with a course of fifteen to twenty-five injections of insulin, the doses being regulated for each child so that the symptoms of shock were not too severe. Most children were at least temporarily benefited — even those treated at home with no change in environment. This improvement was attributed to secondary endogenous production of adrenaline, which improved the asthmatic symptoms. Others have also claimed improvement of asthma by the use of insulin shock therapy.

The evidence cited so far does not show that a low blood sugar level is a cause of the asthma attack. The figures of Malone[44] and Black[45] do not fall below 70 mg. per 100 cc., which is generally accepted as the point below which a state of hypoglycemia exists. Falling blood sugar values after allergic shock could also occur in almost any other type of shock. How low is the blood sugar level at the onset of a nocturnal attack of asthma? Patients with asthma who miss a meal during the day probably have a fall in blood sugar but do not necessarily suffer an acute attack of asthma.

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Although blood sugar levels in patients have not been reported at the time when a severe attack occurs, these persons are often unable to eat, and consequently the blood sugar must fall; this, however, is a result rather than a cause of the asthma. Again, why should injections of insulin or insulin-shock therapy improve asthma when the effect is a hypoglycemia? There is no proof that such improvement does take place; Joseph's[49] patients probably gained in health because of a better appetite. No regular schedule of injections of insulin was maintained, levels of the blood sugar were not followed regularly, no glucose tolerance tests were done, and some patients had other forms of treatment as well. Thus, the answer to the causes of asthma is not likely to be concerned directly with the blood sugar level.

Cholesterol and Fat Metabolism

Cholesterol is an essential constituent of all cells and fluids of the body. It is concerned with the metabolism of fat, and a disturbance in the metabolism of fat has been considered a factor in the cause of eczema. In 1933 Hansen[52] studied the blood content of cholesterol and fatty acids in 5 normal infants and in 6 infants with eczema. The levels of cholesterol and total fatty acids in the blood serum were slightly less in the cases of eczema than in the control infants, although still within the normal range. The average iodine number of the serum fatty acids in the eczema group was 84, and in the control group 111, indicating that the serum fatty acids were less unsaturated in infantile eczema than in the control infants. The author assumed that unsaturated fatty acids played a role in the etiology of infantile eczema. In 1936 Bullen and Bloor[53] determined the total fatty acids, the cholesterol fatty acids and the iodine number — by the same method that Hansen[52] had used — on 14 patients with hay fever or asthma who also had had eczema in infancy and on 12 nonsensitive subjects in the same age group. The averages of the results were nearly identical in the two groups. There was no definite difference in the degree of unsaturation of the plasma fatty acids. Thus, the feeding of unsaturated fats appears to be of no therapeutic value in asthma and hay fever. Bloor, Blake and Bullen[54] then did further work on the fractions of the total fatty acid, neutral fat, phospholipids and cholesterol esters in 14 patients with asthma, 11 with hay fever, 1 with contact dermatitis and 1 with chronic urticaria, as well as in 5 normal persons. No definite differences were found in the nature of the fatty acids in the three classes of sensitive patients and in the nonsensitive subjects. On the other hand, marked differences were observed in the degree of unsaturation in the three groups of compounds. In the cholesterol esters the fatty acids were much more unsaturated than in the phospholipids or in the neutral fat, and in the phospholipids the fatty acids were somewhat more unsaturated than in the neutral fat. Cholesterol appears to have a special function in the metabolism of the unsaturated fatty acids, but what this is and what it has to do with allergy the authors do not state.

In 1937 Bruger and his collaborators[55] determined the levels of cholesterol in the bloods of 49 patients with hay fever and 50 patients with asthma under treatment. They found that there was a tendency for the total blood cholesterol to be slightly elevated above the average normal in patients with treated hay fever and slightly below normal in those with treated asthma. In both groups the percentage of free cholesterol in total cholesterol was definitely elevated above the average normal. In 1938 Chobot and Dundy[56] measured the levels of cholesterol in the blood of 35 allergic and 25 nonallergic children and observed that 12 allergic children had values above 200 mg. per 100 cc. Since a high blood cholesterol may suggest hypothyroidism, they tried therapy with desiccated thyroid in these children but produced no benefit.

Since the metabolism of cholesterol is so little understood, it would be difficult to say on the evidence at present available that cholesterol is concerned with allergy. The idea that the fat metabolism is concerned with the fundamental nature of allergic sensitivity is an attractive thought, but it cannot be supported as yet. A paper by Burr has suggested that the feeding of linseed oil, which contains predominately unsaturated fatty acids, to infants with atopic eczema is beneficial. This treatment has been given to only a few patients so far, but in most of these the eczema has been improved, and the method deserves further study. One notes that except for Hansen's report, the work on fats in allergy has been done on patients with asthma and hay fever rather than on patients with eczema.

The Vitamins

Vitamin C

Another attractive theory about the causes of allergy has been that vitamins play a part — either a deficiency in feeding or a faulty absorption and utilization. Ascorbic acid is a reducing agent and is believed to function as a respiratory catalyst in oxidation phenomena in the cells of the body tissues. In 1936 Solomonica[57] claimed that vitamin C administered prior to sensitization with horse serum protected guinea pigs against anaphylactic shock. In contrast, however, Dragstedt, Eyer and Ramirez[58] failed to show that vitamin C protected dogs against peptone shock or against anaphylactic shock after sensitization with horse serum. In a series of experiments with guinea pigs Van Niekerk[59] concluded that a deficiency of vitamin C had no influence on the development of anaphylactic sensitization to horse serum. Preliminary

treatment with vitamin C did not protect the animals against shock, nor did the addition of vitamin C to the horse serum hamper the shock action. In a different experiment Cohen[60] reported that vitamin C deficiency induced by feeding 25 guinea pigs only 20 to 64 per cent of the daily requirement did not prevent the development of anaphylaxis.

Beginning about 1938, ascorbic acid was used rather widely in the treatment of patients with allergic symptoms. Hunt[61] treated 25 patients with asthma with 100 mg. of ascorbic acid daily for several weeks; those with acute symptoms were given 500 mg. parenterally. In no case was any improvement noted in the amount of wheezing, in the incidence of attacks or in the general condition. In 1941 Goldsmith, Ogaard and Gowe[62] found the fasting blood level of ascorbic acid in 29 patients with bronchial asthma to be 0.410 ± 0.051 mg. per 100 cc., a subnormal level being found in 19 cases; the level in a control group was 0.602 ± 0.049 mg. per 100 cc. During a period of several months on a standardized regimen 6 of 7 patients with bronchial asthma were unable to maintain a blood ascorbic acid level of 1.0 mg. per 100 cc. or more, whereas members of a control group maintained such a level in most cases. These findings were interpreted as indicating that there is an increased requirement for vitamin C in patients with asthma.

In 1942 Holmes and Alexander[63] found the urinary output of vitamin C in 25 patients with hay fever (10 mg. per 100 cc.) to be below the amount excreted by average healthy persons (30 to 50 mg. per 100 cc.). This indicated a low level of vitamin C in the body, which was probably due to inactivation or destruction of the vitamin. On treatment with 100 to 500 mg. of vitamin C daily 88 per cent of the patients reported a gain in health. Pollen counts continued to be high during the period of study. Hebald[64] treated 9 proved cases of hay fever with 500 mg. of vitamin C daily and noted no beneficial effects. He did no determinations of the vitamin C levels in blood serum and urine, and the patients had no other form of treatment at the time the study was done. Friedlaender and Feinberg[65] treated 43 patients with hay fever with 500 mg. of vitamin C daily and observed no beneficial results. Blood levels of vitamin C were determined on patients with and without vitamin C therapy, and were found to be within the normal range. Large doses of vitamin C produced the usual saturation blood levels of 1 mg. per 100 cc. Ruskin,[66] in 1945, reported 27 cases of hay fever and asthma treated in 1944 with 250 to 750 mg. of vitamin C daily by mouth. Of these, 20 (74 per cent) were improved, although the pollen count was higher in 1944 than in 1943. Nine of 11 patients receiving desensitization also reported that their symptoms were milder while they were taking the vitamin C. The author concluded that vitamin C was valuable in allergy — even superior to desensitization — and that allergic disturbances were related to nutritional deficiencies, primarily that of ascorbic acid.

Niacin is believed to be a component of coenzymes that act in glycolysis and cellular respiration. It also acts as a vasodilator and increases circulation of the blood. In 1941 Maisel and Somkin[67] treated 21 patients having severe asthmatic paroxysms with 0.1 gm. of niacin intravenously and produced relief of symptoms in 16 patients. Of 9 chronic asthmatic patients who received 0.2-gm. doses of niacin orally, 5 were benefited. The authors did not know the exact mechanism of action of the niacin in these cases, but they had no reason to believe that a vitamin deficiency existed. In 1943 Melton[68] gave 50 or 100 mg. of niacin intravenously to 19 patients during acute paroxysms, with definite improvement in 16 cases. The drug was also given orally in doses of 50 to 100 mg. two or three times daily to 30 patients who had frequent paroxysms. Frequency and severity of attacks were reduced in 16 cases. Flushing and other symptoms produced by niacin appeared in some cases. The author thought that the action of the drug in dilating blood vessels was accompanied by a similar action on the bronchioles.

In general, then, one must observe that patients with asthma are often undernourished and require an increased amount of vitamins for recovery of general health. In addition, it must not be forgotten that in other conditions in which metabolism is increased, such as prolonged exercise, burns and chronic debilitating diseases, more vitamins are required by the body. Many nonallergic persons with low levels of vitamins in the body experience a gain in health on treatment with large doses of these vitamins. Ruskin[66] did not mention a control series of cases treated by desensitization alone: he did not discuss the general health of the patients, their dietary habits or changes in weather. His proof that vitamin C therapy in these patients was the dominant factor in the improvement is therefore not conclusive. The action of niacin in asthma does not seem to be on a basis of vitamin deficiency, but is possibly due to its vasodilator effect. Deficiencies of vitamin C or niacin, then, are probably not contributory causes of asthma, but when present they may aggravate asthma, which already exists.

Other Causes of Asthma

In 1940 Evans and Bodman[69] developed an interesting theory — that the cause of allergic manifestations involved the absence of certain catalysts of coenzyme activity. By using an oxidation catalyst — ethylene disulfonate — they attempted to restore the deficiency. They had no objective findings to confirm their theory, and the treatment recommended — ethylene disulfonate — has been shown to be worthless.

Another concept about allergy is much more interesting. In 1936 Selye[70] presented his theory of the adaptation syndrome, which may be defined briefly as the response of the organism to stress or damage to which it is not adapted. The first or shock phase when the patient is subjected to the alarming stimulus is characterized by tachycardia, a decrease in muscular tone and body temperature and a rise and then a fall in the blood pressure and in the blood sugar. There is anuria, acidosis and a discharge of adrenaline from the adrenal medulla. With these go certain other changes, such as hemoconcentration, edema formation, leukopenia followed by leukocytosis, negative nitrogen balance and chemical changes in the blood, including an increase in nonprotein nitrogen, potassium, phosphate and globulin and a decrease in the blood chloride. The shock phase is followed by the countershock phase in which the subject begins to develop resistance to the damaging agent. There is enlargement of the adrenal cortex and a general reversal of the changes occurring in the shock phase, with an increase in production of corticoid hormones from the adrenal cortex accompanied by a decrease in urinary excretion of 17 ketosteroids. Thirdly, there is the stage of resistance, and finally the stage of exhaustion. Selye[71] calls conditions in which these changes occur "diseases of adaptation" and cites as examples hypertension, nephrosclerosis, rheumatic fever, periarteritis nodosa and gastrointestinal ulcers.

This idea of Selye is pertinent to the asthma problem. There is no doubt that asthma is often a reaction to stress and strain. The only difficulty is that the objective findings, particularly the chemical changes observed in asthma, are not always the same as those described by Selye for his adaptation syndrome. The problem is being studied further.

Williams[72] put forward the hypothesis that physical or intrinsic allergy (Ménière's disease) is a disorder of the normal alarm reaction and that there is an inherited disorder of certain localized cells in which, in response to certain normal stimuli, the cells are unable to utilize the normal amount of adrenal hormones available to counteract the histamine released, or else too much histamine is released for the amount of available adrenal hormone to counteract.

* * *

It will be noted that none of the investigations reviewed above have greatly helped an understanding of the fundamental basis of allergy. Most of the chemical changes observed in allergic disorders seem to be results of these conditions rather than causes of them.

The theory that treatment with potassium improves patients with allergic disorders has not been generally accepted, and such therapy does not seem to be of great value. When disturbances of water balance occur, they should certainly be corrected. A study of the total balances, — that is, the total intake as compared to the total output, of sodium, potassium and water in the body, — together with the use of radioactive materials, may reveal more accurately than simple blood levels any shift of these substances in the cells and tissues of the body that may occur in allergy.

Therapy with calcium or magnesium is not specific for allergic conditions and is not indicated unless an actual deficiency of these substances in allergic patients is proved. So far as blood sugar is concerned, it would be interesting to know if it is at a low level at the onset of nocturnal attacks of asthma; if this can be shown, carbohydrate feedings before retiring at night may benefit some patients. Insulin shock seems to be justified only when psychiatric factors are dominant in aggravating the symptoms.

Since the metabolism of cholesterol and fat is not well understood in the normal person, it is hard to say whether a disturbance exists in allergic patients, although this does not seem likely on the evidence so far available.

Deficiencies of ascorbic acid or niacin cannot be incriminated as causative factors in allergy. There have been few reports on the functions of the other vitamins in allergic disorders, but from what is known about these vitamins at present it does not seem likely that any of them are specifically concerned. Perhaps a new vitamin will be discovered that may turn out to be of vital importance in allergy. Meanwhile, all patients suffering from chronic diseases should be properly fed, and the diet should include adequate amounts of all the known vitamins, with extra quantities if a deficiency exists.

Finally, few of the changes occurring in the body during the alarm reaction have been found in asthma. There have been no conclusive reports, however, on the blood chloride, on the blood globulin or on nitrogen metabolism in asthma. Studies of these factors ought to reveal whether or not asthma, eczema and kindred diseases belong with Selye's "diseases of adaptation." Studies of the function of the adrenal cortex in asthma are also needed.

From this review of investigations in chemical changes in allergy, it is obvious that in any future work strict attention must be given to exact methods, technics and controls, since the status of asthma depends on many variable factors.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 33371

PRESENTATION OF CASE

First admission. A forty-three-year-old housewife entered the hospital because of generalized arthritis.

At the age of eighteen years the patient had had mild "rheumatism" in the legs, wrists and hands. Two years before entry the toes became swollen and painful, followed by similar involvement of the ankles and knees, the right knee more so than the left. The elbows, shoulders, jaws, hands and the spine then became affected at one time or another, and there had subsequently been a constant ache in the cervical spine. Occasionally, the joint symptoms were accompanied by fever. A year before entry the patient became unable to walk. She spent three months at a local hospital but obtained no relief, despite tonsillectomy and adenoidectomy. While she was there the eyes became red and lachrymose and began to ache. She could not read because of blurred vision. At the time of entry the hands, wrists and cervical spine were the source of the greatest discomfort. The aching pain was somewhat relieved by aspirin. The patient had lost 18 pounds since the onset of the illness.

Physical examination revealed a pale, obese woman showing evidence of weight loss and moving with difficulty because of stiff joints. There were scattered telangiectases over the cheeks. The eyes showed lacrimation, photophobia, "bluish" scleras, moderately deep ciliary injection and many vitreous opacities. There were also some healing marginal infiltrates at the nasal border of the right cornea and several small, firm, gelatinous-appearing nodules in the conjunctiva of the left eye just above the insertion of the external rectus muscle. The fundi were normal so far as could be determined through the medial haze. The neck and spine were stiff. The lungs were clear. The heart was not enlarged to percussion. A harsh, low-pitched systolic murmur was heard over the entire precordium, loudest in the aortic area. The aortic second sound was absent. There was a moderate systolic blow at the apex. The abdomen was normal. The temporomandibular joints, shoulders, elbows, wrists, fingers, knees, ankles and toes were stiff and limited in motion, with enlargement, irregularity and tenderness. The fingers were tapering and spindle shaped. Scattered, small, tender subcutaneous nodules were found over the extremities, particularly at the elbows.

The temperature was 99.8°F., the pulse 105, and the respirations 22. The blood pressure was 140 systolic, 90 diastolic.

Examination of the blood disclosed a red-cell count of 4,340,000, with a hemoglobin of 70 per cent, and a white-cell count of 7800, with 95 per cent neutrophils. The total serum protein was 8.3 gm. per 100 cc., with 4.0 gm. of albumin and 4.3 gm. of globulin. The sedimentation rate was 1.47 mm. per minute. A blood Hinton test was negative.

A Congo-red test showed 100 per cent retention of the dye in the serum. The urinary sediment contained numerous white cells but was otherwise negative. A phenolsulfonephthalein test showed 50 per cent excretion of the dye in one hour.

On x-ray examination the heart was at the upper limits of normal. The lungs were clear. There was irregular destruction of the joint surface of the majority of the metacarpal, carpal, interphalangeal and phalangeal joints. The adjacent bone was markedly decalcified. No bony fusion was apparent, but there was slight subluxation in the first metacarpophalangeal joint. The feet showed similar changes. There were areas of subchondral destruction in the elbow and knee joints. The sacroiliac joints and spine disclosed no evidence of involvement. The sinuses were normal. There was marked caries, with apical abscess formation about the first left lower molar and the first left upper molar bicuspids. An electrocardiogram was normal.

The patient did well on aspirin, mild sedation, leg casts, raw liver and general supportive measures, with gradual simultaneous improvement in both joint and ocular symptoms. A biopsy of one of the subcutaneous nodules from the right elbow was reported as showing a "rheumatic nodule, probably rheumatoid." After three months in the hospital a definite soft aortic diastolic murmur appeared, and a low-pitched late diastolic rumble was thought to be present at the apex when the patient was lying on the left side.

Another electrocardiogram showed a greater shift to the left of the electrical axis than did the previous record. The sedimentation rate was 1.48 mm. per minute. After four months in the hospital the patient was cystoscoped because of continued pyuria. Stones were found in the left ureter, and a left ureteromeatotomy was done to facilitate their passage. An intravenous pyelogram showed normal excretion of the dye bilaterally. On discharge after six and a half months in the hospital the patient had regained sufficient strength to walk 10 or 15 feet. At times she still had considerable pain in the knees and ankles. Objectively, the joints showed little change. The eyes were symptomatically improved, but the patient was unable to read because of the medial opacities.

Final admission (seven years later). After discharge the patient continued to feel much better, although the limitation of motion progressed slowly. Nevertheless, she was able to use a "walker" until one year before entry, when she had an acute exacerbation following a minor emotional upset (an altercation with a maid). Some months later several "abscessed" teeth fell out, and the right ear became painful, with perforation of the eardrum. At about the same time the ankles began to swell and five months before entry a physician noted an enlarged spleen and a slight amount of abdominal fluid. The edema and ascites gradually progressed. Three paracenteses were performed, each productive of about 4000 cc. of fluid.

Physical examination revealed massive edema from the feet to the lower chest. The pupils were slightly irregular; the right was larger than the left. Both nasal cavities were filled with dry bloody crusts. The lungs were clear, except for occasional rales at the bases. The border of the heart extended 13 cm. to the left of the midsternal line in the fifth interspace. A harsh Grade III systolic murmur was heard over the entire precordium, but best over the midsternum in the third interspace. A Grade II, high-pitched diastolic murmur was loudest at the left sternal border in the third interspace. The spleen was ballotable five fingerbreadths below the costal margin. The liver edge was not felt, but by percussion it was two fingerbreadths below the costal margin. There was marked ascites. All the joints of the extremities showed progression of the arthritis, with marked limitation of motion and some subluxations.

The temperature was 99°F., the pulse 88, and the respirations 20. The blood pressure was 128 systolic, 60 diastolic.

Examination of the blood showed a red-cell count of 4,600,000, with 12.2 gm. of hemoglobin, and a white-cell count of 4500, with 82 per cent neutrophils. The serum protein was 4.4 gm. per 100 cc., with an albumin of 1.3 and a globulin of 3.2 gm. The nonprotein nitrogen was 79 mg., the serum cholesterol 250 mg. and the cholesterol esters 178 mg. per 100 cc. The corrected sedimentation rate was 1.85 mm. per minute. A Congo-red test showed 46 per cent retention of the dye in the serum. The cephalin-flocculation test was ++ in twenty-four and +++ in forty-eight hours. The thymol turbidity was 6.0 units. The urine was acid and had a specific gravity of 1.020. It gave a ++++ test for albumin. The sediment contained occasional hyaline casts and 15 to 20 white cells per high-power field.

An x-ray film of the chest revealed some prominence of the heart in the region of the left ventricle, with a cardiothoracic ratio of 16:31. There was a small amount of fluid in the right pleural sinus.

An electrocardiogram showed sinus rhythm. The rate was 75. The PR interval was 0.16 second, and the QRS complex 0.06. There were notched, low P waves and inverted T waves in Leads 1 and 2 and a flat T wave in Lead 3. The QRS complexes in Lead CF_2 were normal. The T wave in Lead CF_4 was inverted, and that in Lead CF_5 slightly inverted.

Despite the administration of Mercupurin, the patient excreted less than 500 cc. of urine a day. An abdominal paracentesis produced 4000 cc. of cloudy-yellow fluid, with a specific gravity of 1.006. It contained many diplococci and 250 cells per cubic millimeter, 90 per cent of which were mononuclear forms. The patient gradually became hyperpneic,

lapsed into coma and died on the ninth hospital day.

Differential Diagnosis

Dr. Alfred O. Ludwig: There seems to be no doubt that this woman suffered from severe, progressive rheumatoid arthritis, which had persisted for a number of years, in fact since the age of eighteen. The particular points of interest in this case are the various complications that accompanied the disease. At the onset of the illness, the history indicated that she had the exacerbations and remissions that are common in rheumatoid arthritis in the early stages. Such episodes are frequent until the disease becomes chronic; on the other hand, it may become chronic from the start.

It is of particular interest that the patient had some lesions in the eyes. From the description given I suspect that these were due to episcleritis, which frequently occurs as a complication of rheumatoid arthritis. I believe that the pathologic picture was that of a rheumatoid nodule in this area. Another ocular complication of rheumatoid arthritis is iritis, of which there was no evidence in this case.

The physical examination at the first entry was characteristic of generalized and severe rheumatoid arthritis. It is interesting that at the examination on the first admission there was no aortic diastolic murmur — only a harsh, low-pitched, systolic murmur, which I am inclined to interpret as important clinically and about which I shall say more later.

Tender subcutaneous nodules are common in rheumatoid arthritis and occur most frequently over the elbows. They are similar to those found in rheumatic fever. They may also be found over the knees, over the lateral surfaces of the ulna and occasionally in other places. I believe that they are present in about 20 per cent of cases of rheumatoid arthritis. Their pathology differs somewhat from that seen in the nodules of rheumatic fever.

The temperature, pulse and respirations do not help us much. There was a slight degree of anemia at that time. It is significant that the total protein was increased to 8.3 gm. per 100 cc., and that there was an increase of the globulin fraction to 4.3 gm. I might say here that hyperproteinemia and hyperglobulinemia are not unusual findings in rheumatoid arthritis. I cannot explain why this occurs. It bears some relation to the rapid sedimentation rate seen in certain cases, although it does not explain entirely the increased sedimentation rate. Occasionally, one sees the increased globulin reflected in the spinal fluid as well, and in such cases a strongly positive gold-sol curve of the paretic type may also be found. The blood Hinton and the spinal-fluid Wassermann reactions in such cases are negative. The total protein may also be increased in the spinal fluid as a reflection of this change in the blood. This is particularly important in patients in whom the sacroiliac joints are involved, and such lesions may be confused with ruptured intervertebral disks.

At that time there was no abnormality in the Congo-red test. Whether or not the presence of white cells in the urine was significant, I do not know. We are not told whether this was a catheterized specimen. The phenolsulfonephthalein test was normal.

It is interesting that after three months of hospitalization a definite aortic diastolic murmur appeared. Someone thought that he heard a low-pitched, late, diastolic rumble at the apex, which suggests that there was definite valvular involvement of the heart, with lesions of the aortic and mitral valves. What does that mean in a case such as this? Here is a patient with apparently definite rheumatoid arthritis involving most of the joints who developed findings in the heart that are consistent with rheumatic heart disease, or at least are those that one usually associates with it. A number of cases have been described in which heart lesions of this sort occurred coincident with chronic rheumatoid arthritis.* These lesions are predominantly located on the aortic valves. We also have seen such cases in this hospital. I do not know whether or not the histology of this type of endocarditis differs from that found in rheumatic fever.

It is also interesting that the electrocardiogram showed a greater left-axis deviation than previously. The sedimentation rate, of course, was greatly elevated, the normal being 0.35 mm. per minute.

It was thought necessary to cystoscope this patient because of continued pyuria. Apparently, the white cells previously reported in the urine were important. Stones were found on that examination, which raises the question how the stones got into the left ureter. Two possibilities suggest themselves. In the first place, this patient, like all patients with severe chronic rheumatoid arthritis, had a great deal of decalcification and, therefore, undoubtedly excreted much more calcium in the urine than normally. Furthermore, she had a urinary infection. Whether the infection preceded and therefore contributed to the stones or whether it followed the stones, I do not know. At that time she still did not show any decrease in renal function. It is obvious that she had not really made any great clinical progress after the long period of hospitalization.

At the second admission the important points were the appearance of edema of the ankles, an enlarged spleen and the presence of abdominal fluid. From that time on, both edema and ascites increased steadily to the point where three abdominal paracenteses had to be done. Examination confirmed this finding of massive edema from the chest down. I cannot believe that the irregularity of the pupil

*Baggenstoss, A. H., and Rosenberg, E. F. Cardiac lesions associated with chronic infectious arthritis. *Arch. Int. Med.* 67:241-258, 1941.

was important, except that it may have been evidence of a previous iritis. The heart border extended 13 cm. to the left. That is significant, but one cannot be certain that the enlargement was not apparent and due to increased abdominal fluid, which pushed the heart up and out. The murmurs had definitely changed. There was a Grade III systolic murmur over the precordium, heard best over the mediastinum, and a Grade II, high-pitched aortic diastolic murmur, loudest at the left sternal border, the position in which one usually expects to hear aortic murmurs best. Both the spleen and the liver appeared to be considerably enlarged. The joint lesions had shown continued progression.

The laboratory findings are of some importance. There was still a slight degree of anemia. This and the diminution of the white-cell count occur in rheumatoid arthritis. The leukopenia was part of what has been described as Felty's syndrome — a clinical picture consisting of leukopenia, splenomegaly and lymphadenopathy in association with rheumatoid arthritis. The serum protein was below normal, but there was still a marked increase in the amount of globulin, with reversal of the albumin-globulin ratio. The nonprotein nitrogen was elevated to more than twice the normal, and there was also an increase in the cholesterol and cholesterol esters. The sedimentation rate was as high as before. I do not believe that the Congo-red test was significant. The cephalin-flocculation and the thymol-turbidity tests, as well as the increased globulin level in the serum, are used to aid in the diagnosis of decreased liver function. The urinary findings improved. There was marked albuminuria, with presumably a good specific gravity — if the patient could concentrate to 1.020, she had not lost much renal function.

I shall have to ask a cardiologist to interpret the electrocardiogram.

The final course showed increasing oliguria. Abdominal paracenteses continued to produce large amounts of fluid. We are told that the fluid became infected. Diplococci and leukocytes were found in it, so that the patient was developing or had already developed a low-grade peritonitis, presumably due to a pneumococcus. This is not infrequent with nephrosis and is not rare as the terminal event with this complication. The hyperpnea I explain on the basis of acidosis from increasing renal failure.

There are several perplexing points about the case. What other possibilities might account for these complications? We have a good deal of evidence that this patient had rather extensive amyloid infiltration, including an amyloid nephrosis. The renal findings were consistent with it, as was the Congo-red test and the enlargement of the liver and spleen. There are other things, however, that may have been implicated. The patient may have had a sufficient degree of impaired liver function with cirrhosis to account for the ascites, although I do not believe from the information at hand that one is justified in drawing that conclusion.

Finally, is it necessary to assume any serious degree of heart failure to account for the production of ascites? I do not believe from the clinical findings that this is so. Nor is there sufficient evidence to say that there was impairment of the venous return to the heart. One might consider a tricuspid lesion, of which I cannot see any evidence. So far as the kidneys are concerned, one cannot forget that the patient had renal infection, pyelitis and pyelonephritis, which may also have contributed to the eventual breakdown of renal function. Before we go farther, it would be wise to see if the x-ray film will help and also to ask the cardiologists to interpret the electrocardiographic findings.

Dr. Stanley M. Wyman: Unfortunately, the films of the first examination are no longer available. This film of the chest was taken in the supine position, so that accurate measurement of the heart is impossible. The right leaf of the diaphragm is elevated more than usual. The lung fields are clear. The heart shadow may be prominent toward the left. The changes in the hand are those of severe osteoporosis, with loss of subchondral bone in the carpal bones and in the terminal portions of several of the phalanges.

Dr. Ludwig: These x-ray films show extensive destruction around the joints.

Dr. Edward F. Bland: The electrocardiogram shows a digitalis effect on the ST intervals and perhaps evidence of slight left ventricular strain.

Dr. Ludwig: I should be satisfied to leave the diagnosis as extensive, severe chronic rheumatoid arthritis complicated by serositis and by a heart lesion, the nature of which I am not certain. I think it will be demonstrated that there was involvement of both the aortic and the mitral valves and, finally, that there was extensive amyloid infiltration secondary to the rheumatoid arthritis and involving primarily the spleen, liver and kidneys. I also predict that there was some degree of pyelonephritis.

Dr. Bland: We saw this patient repeatedly in 1939 and 1940. We were especially interested at that time in a group of patients with rheumatoid arthritis who also had valvular heart disease. One of this group had a high degree of nonspecific aortitis and aortic regurgitation, which Dr. Mallory was not quite willing to classify at autopsy. This patient, however, does not seem to fit this special group. The cardiac signs began with a systolic murmur, and it was not until considerably later that we also recognized an aortic diastolic murmur. Aortic-valve disease, with predominant stenosis acquired at a relatively early age, always suggests the possibility that an inflammatory lesion has been superimposed on a bicuspid aortic valve. I should like to throw that possibility in. I doubt if she had mitral disease except on a statistical basis.

Dr. Ludwig: On the basis of the type of heart disease that we see in rheumatoid arthritis?

DR. BLAND: Yes.

DR. MARIAN W. ROPES: Regarding the cardiac involvement, I remember that during the first admission there was a good deal of discussion whether both valves were involved. The arthritic group thought more strongly than the cardiac group that the patient had mitral as well as aortic disease, but it was so questionable that our final diagnosis was similar to Dr. Ludwig's. We were disturbed by the features of the terminal illness. I thought that she had an early onset of extreme ascites predominating over the rest of the anasarca throughout the several months, and no evidence of congestive heart failure, and during the period in which I studied her, it seemed that there was no definite evidence of anything in the region of the portal system or inferior vena cava to explain this. The Congo-red retention is interesting in that I thought it was higher than one might expect in what we analyze as severe amyloidosis. She did have iritis early in the disease, and she had nodules at one stage.

CLINICAL DIAGNOSES

Rheumatoid arthritis.
Amyloid nephrosis.

DR. LUDWIG'S DIAGNOSES

Rheumatoid arthritis, chronic, severe.
Chronic endocarditis, with involvement of mitral and aortic valves.
Amyloidosis.
Pyelonephritis.

ANATOMICAL DIAGNOSES

Rheumatoid arthritis.
Rheumatic heart disease, with mitral and aortic stenosis.
Splenomegaly.
Nephrosis.
Anasarca.
Pulmonary edema and congestion.

PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: Dr. Ludwig has made a convincing case for generalized amyloidosis. I do not see how anyone can doubt it on the basis of this history, but this patient did not have it. Autopsy disclosed characteristic rheumatic heart disease, involving both the aortic and the mitral valve, with a fairly severe grade of stenosis of both valves. The lungs showed chronic passive congestion and a moderate degree of pulmonary edema. The liver showed no passive congestion whatever, which I think is fairly strong evidence against heart failure as a cause of the ascites and edema. The spleen was greatly enlarged, weighing 900 gm. Grossly, we were quite sure that it contained amyloid, but on microscopical examination there was not a trace of it. It was a rather large, fibrous spleen suggesting more closely what one sees with portal hypertension — the so-called "Banti syndrome" — than any other picture. The sinusoids were dilated, fibroblasts in the pulp cords were definitely increased in number, and the red cells were somewhat diminished in number. The kidneys were slightly enlarged, weighing 450 gm. The surfaces were quite pale. They seemed somewhat dark on gross examination, and again we thought that they were consistent with amyloid involvement. On microscopical examination the glomeruli, the blood vessels and the interstitial tissues were entirely free from amyloid. There was a rather severe grade of albuminous degeneration of the tubules, a simple nephrosis of the idiopathic type. There was little evidence of pyelonephritis. The renal lesion was, I think, quite adequate to explain the marked degree of albuminuria and the nephrotic syndrome.

DR. ALFRED KRANES: Why was the spleen enlarged?

DR. MALLORY: Once in a while, in rheumatoid arthritis, we see large spleens that we cannot explain on any other basis than this syndrome, if one wishes to use that term.

DR. BLAND: Could you tell us whether the aortic valve was bicuspid?

DR. MALLORY: We did not think so.

CASE 33372

PRESENTATION OF CASE

First admission. A fifty-six-year-old Italian telephone worker was admitted to the hospital because of cough.

He had been well until two months previously, when he developed a nonproductive cough. He later had what a physician diagnosed as "grippe," which was characterized by cough and expectoration, a temperature up to 102°F. and pain in the left lower anterior portion of the chest. He was in and out of bed for ten days. The temperature responded to penicillin, and he finally went back to work. An x-ray film taken at that time, however, showed density in the right lower portion of the chest near the anterior end of the seventh rib and a larger patch of density in the left upper portion of the chest, extending outward from the hilar region and into the apex. Because of these findings the patient was advised to enter the hospital.

There was no history of a recent tonsillectomy, tooth extraction or inhalation of a foreign body.

Physical examination revealed only dullness, with decreased fremitus and voice sounds in the left upper portion of the chest.

The temperature was 99°F., the pulse 90, and the respirations 20. The blood pressure was 190 systolic, 80 diastolic.

The urine showed a ++ test for albumin and an olive sugar test. The fasting blood sugar was 267 mg. per 100 cc., but on a special diet it was

brought to a steady level of 123 to 143 mg. The hemoglobin, white-cell count, differential count, serum nonprotein nitrogen, total protein and carbon dioxide were within normal limits. Repeated sputum examinations were negative for tubercle bacilli. A chest film revealed an area of increased density extending upward from the left lung root into the apical division of the left upper lobe. There was a 5-cm., ragged cavity within it that seemed to have a fluid level. The left leaf of the diaphragm was elevated but moved freely. There was a small amount of fluid in the left pleural sinus. The left upper lobe was not much reduced in size. The right lung was clear. Two bronchoscopic examinations disclosed constriction of the left upper-lobe bronchus, but both biopsies and smears were negative for carcinoma.

The patient was discharged on the eighteenth day.

Second admission (one month later). The patient was readmitted with fever, chills and dyspnea. In the interval he had felt reasonably well except for persistent cough and expectoration of about a cupful of sputum a day, which was blood streaked on occasions. He continued to have pain off and on in the left anterior portion of the chest, along with some substernal pressure, but this was not related to exercise, cough or deep respiration. There was no appreciable weight loss. One day before admission he had dyspnea, chills and fever.

Physical examination showed no change from those on the first admission.

The temperature was 103°F., the pulse 100 and the respirations 23, but these were readily controlled with penicillin therapy.

Examination of the blood revealed a white-cell count that varied from 14,800 to 10,000. The fasting blood sugar was 121 to 139 mg. per 100 cc. The blood chemical findings were otherwise normal.

X-ray examination showed some increase in the size of the cavity in the left upper lobe and some elevation of the left leaf of the diaphragm.

A third bronchoscopy showed only constriction of the left upper-lobe bronchus; the biopsy was negative for carcinoma.

An operation was performed on the twenty-third hospital day.

Differential Diagnosis

Dr. Lowrey F. Davenport: Since most of the findings, including the sputum examination and bronchoscopy, were negative, our chief reliance is on the serial x-ray films, and I should like to request that they be shown.

Dr. Stanley M. Wyman: The cavity discussed lies in the apex of the left upper lobe medially. It can be distinctly seen in the lateral view. There is some density throughout the apical portion of the left upper lobe. Elevation of the left leaf of the diaphragm is well seen in the entire series. A film taken twelve days later shows a definite fluid level in the base of the cavity, but no other essential change. In a film taken a month later the cavity appears to be considerably larger, with again a small fluid level in its base. A film taken two weeks later shows no definite change except for some decrease in the reaction around the ring shadow. There is, however, one thing to add to this report — that is, what appears to be a small nodule in the right lower-lung field. This is present only on the film taken at the last examination.

Dr. Davenport: Two months prior to the first admission this fifty-six-year-old man presented symptoms of a respiratory infection — fever, cough and sputum. The subsequent course on the two hospital admissions and the serial x-ray films suggest a destructive process involving the left upper lobe. We are faced, as we always are in these cases, with the problem of trying to differentiate simple lung abscess and abscess complicated by tumor or some chronic type of inflammatory process, such as tuberculosis. I believe that it is to these three possibilities only that we should give our serious attention.

Confusing things about symptomatology often arise now that the antibiotics, such as penicillin, have become available. We have often been misled by the thought that a definite — sometimes a dramatic — response in temperature, white-cell count and the site of the x-ray shadow following penicillin are evidence against the possibility of an underlying tumor. We should remember that if there is bronchial obstruction with underlying suppuration the inflammatory reaction secondary to the bronchial obstruction can be influenced markedly by penicillin and the various sulfonamides. The facts that the original episode of so-called "grippe" responded to treatment and that the symptoms of inflammation at the time of the first admission responded to penicillin therapy are of no help in reassuring us regarding the inflammatory nature of the process.

Always, when a patient presents glycosuria, as in the case under discussion, and an elevated blood sugar, we must be on the lookout for the bizarre forms of tuberculosis. Tuberculosis in a diabetic patient is notoriously difficult to diagnose in some of the early stages because it does not behave according to the usual pattern. It starts out with a fulminating process, with inflammation and an acute exudative process similar to acute lobar pneumonia, and may excavate readily. But in a patient in the hospital for as long a period as this patient was, with repeated sputum examinations and a cavity as large as this, in whom no tubercle bacilli have been found in repeated searches, it is reasonable to exclude tuberculosis. Occasionally in tuberculosis sanatoriums we see cavities with negative sputum on persistent examination. Most of them are observed in cases of chronic productive tuberculosis in which the cavity has epithelialized. I cannot conceive of tuberculosis in such a rapidly destruc-

tive process as this without innumerable tubercle bacilli in the sputum.

Could this have been a simple lung abscess that had been held more or less in abeyance by sulfonamide therapy and antibiotics? There are several points in the history against the possibility that this was the type of abscess that follows tooth extraction, foreign body or toxemia. The rapidity of excavation and the type of sputum were much against it. Also, bronchoscopy gave chiefly negative evidence but one bit of helpful data: although there was no evidence of growth in the bronchus, constriction of the left upper-lobe bronchus was noted on both occasions. If this had been tuberculosis of a rapid fulminating nature, constriction on a tuberculous basis could not have taken place so quickly. Nor, in simple lung abscess, would one expect constriction, even though the bronchoscopic findings were essentially negative.

The report on two occasions that there was constriction of the bronchus in the left upper lobe makes me lean definitely to the diagnosis of primary bronchiogenic cancer, with bronchial obstruction, suppuration and excavation. That brings us up to the method of handling these cases. Before the days of chemotherapy when the chest was opened with fear, and before pneumonectomy and lobectomy were being done, we studied some of these patients overzealously, trying to establish the diagnosis between a simple lung abscess, tumor and inflammatory, nontuberculous and tuberculous processes. We now believe that it is wise to excise a localized destructive process in the lung, whether benign or malignant, suppurative or tuberculous, in the absence of definite evidence of involvement elsewhere. As is well known, more and more frequently we are going ahead in cases of localized tuberculosis and picking primary resection as the treatment of choice. Since I have seen these x-ray films and had the nodule called to my attention, I am somewhat more hesitant about recommending operation because I lean strongly to a malignant process, and if this was a malignant process, with a metastatic nodule already formed at the right base, operation, of course, was hopeless from the standpoint of effecting a cure. This nodule also raises the bare possibility that the left upper-lobe process was not a primary bronchiogenic carcinoma but a metastatic process. I think that that is most unlikely because metastatic nodules rarely cause obstruction and ordinarily do not break down and excavate as the lesion did in this case.

I should have advised operation on the first admission with the tentative working diagnosis of primary bronchiogenic cancer, with secondary excavation due to a blocking process and suppuration.

Clinical Diagnosis

Lung abscess (? carcinoma).

Dr. Davenport's Diagnosis

Carcinoma of lung.

Anatomical Diagnosis

Squamous-cell carcinoma of lung.

Pathological Discussion

Dr. Lamar Soutter: When the chest was entered, innumerable dense adhesions were found over the entire lung. These were freed, and the abscess entered at the apex of the lung, where it was adherent to the upper part of the chest anteriorly. The abscess extended down along the mediastinal vessels and the arch of the aorta into the posterior portion of the chest. The septum between the upper and lower lobes could not be dissected clear because the abscess extended across it. It was obvious that a pneumonectomy would be necessary. Because of the extensive infection along the mediastinum and the large hilar nodes, it was thought that this procedure would be very hazardous; hence, the chest was closed. A catheter was inserted for drainage.

Dr. Benjamin Castleman: A biopsy of the abscess wall showed a well differentiated squamous-cell carcinoma, with marked epithelial pearls and keratinization. This abscess was broken-down tumor rather than a true non-neoplastic abscess beyond an obstructing tumor, which not infrequently occurs in the lung. In this latter group of cases we have seen metastatic cerebral abscesses without metastases from the cancer itself.

A Physician: What was the eventual course?

Dr. Castleman: The patient is still on the ward and receiving x-ray treatment. It is planned to achieve a total dosage of 3000r.

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TETANUS IN THE UNITED STATES ARMY IN WORLD WAR II

Early last year Boyd[1] reviewed the British experiences with tetanus in the African and European theaters of operation, and his report has already been commented on in these columns.[2] Active immunization as employed at first in the British Army consisted of two doses of toxoid, 1 cc. each, about six weeks apart; later a third dose was included in the initial course. An annual booster dose of 1 cc. was also given, and in addition, a single dose of 3000 units of tetanus antitoxin was administered immediately after a wound was sustained in those who had been actively immunized. The same amount of antitoxin was given at weekly intervals to those who had not been immunized. Boyd concluded from his data that tetanus was not entirely prevented by active immunization, since 22 cases occurred in persons who had been actively immunized. Furthermore, although the mortality from the disease was significantly lower in those actively immunized patients who had also received prophylactic antitoxin, in patients who were actively immunized and had not received antitoxin the mortality was not below average. He therefore concluded that the failures were due to a low level of antitoxin at the time of wounding and that this was best remedied by giving antitoxin during the period while the patient was making his own, the best effects being obtained from the early administration of antitoxin.

Corresponding data from the United States Army are now available and are of particular interest because of the differences in the methods employed and in the results attained.[3] In the Army, fluid, not alum-precipitated, tetanus toxoid has been used as an immunizing agent for the prevention of tetanus since 1941. All military personnel received a series of three subcutaneous injections of 1 cc. at intervals of three weeks. A routine stimulating injection of 1 cc. of toxoid was administered one year after the initial series, and an emergency stimulating dose was given on the incurrence of wounds, severe burns or other injuries that might result in tetanus. In addition, a stimulating dose was also given at the time of manipulation of old wounds that were considered as potentially contaminated by *Clostridium tetani*. Before September, 1944, an additional stimulating dose of 1 cc. was given to all persons departing for a theater of operations more than six months after the basic series or the routine stimulating dose; after that time data indicating that this precaution was not necessary had accumulated. At present no further toxoid is given after the routine stimulating dose unless the individual sustains an injury that might result in tetanus, at which time the emergency stimulating dose of 1 cc. of toxoid is administered. Tetanus antitoxin is reserved for the treatment of clinical tetanus and for passive immunization of injured persons in whom there is no evidence of previous administration of toxoid.

Studies were made to determine the levels of antitoxin during the various stages in these im-

munization procedures. It was found that one week after the third injection of the initial series, all specimens contained at least 0.1 unit of antitoxin per cubic centimeter of serum and some contained much more. Since the amount of circulating antitoxin required for protection against tetanus is estimated to be between 0.01 and 0.20 unit per cubic centimeter of serum, it was considered that there was adequate protection immediately after completion of the initial series and that there was no need for prophylactic antitoxin. To determine how long a basic active immunity persists that is sufficient to allow for adequate response to a stimulating dose, a group of persons was studied one year after the completion of the basic course of toxoid. Before administration of the stimulating dose relatively small quantities of circulating antitoxin were present, but one week after this stimulating dose, levels of 0.3 unit or more per cubic centimeter were reached in almost every subject. Comparable results had previously been obtained by Mueller and his associates.[4] In immunized persons who had not received injections of toxoid over a period of from two to five years, only about 10 per cent failed to develop a level of antitoxin that was adequate for protection and the protective levels were produced within a week in all cases. It was therefore considered wise to continue the administration of emergency stimulating doses of toxoid following injury, and it was also thought that an adequate response would then occur within the usual incubation period of tetanus.

Two types of reactions to the toxoid were observed. The first was apparently nonspecific in nature and was manifested by symptoms similar to those that occur after typhoid vaccination, that is, local soreness at the site of injection, headache, general malaise and occasionally chills and fever. These local and general reactions were much less frequent and less severe than those following the injection of typhoid vaccine. The second type of reaction was characterized by the appearance — within thirty minutes — of flushing and itching of the skin or of frank urticaria and occasionally edema of the lips and eyelids. Edema of the glottis and respiratory difficulties were rare. In about 85 per cent of the cases these reactions occurred after the second or third dose, suggesting the production of a hypersensitive state by a previous dose. The majority of the latter type of reactions occurred early in the tetanus immunization program, and it was soon recognized that they were a manifestation of sensitivity to some constituent of the toxoid and that toxoids containing certain types of peptones were the worst offenders. Cessation of the use of toxoids containing these peptones was followed by a decrease in the frequency of these reactions from 63 per 100,000 injections to less than 2. The incidence of reactions resulting from the use of the toxoids now available is extremely low, and reactions from initial injections of these materials are almost nonexistent.

Throughout the entire war period only 12 cases of tetanus occurred among Army personnel, although some other cases may have been overlooked or occurred among wounded soldiers who fell into the hands of the enemy. The 12 recognized cases included 4 that resulted from injuries sustained prior to active duty. Interestingly enough, only 6 of the 12 cases occurred in those who had received the full prophylactic doses, including the emergency stimulating dose of toxoid after injury.

A comparison with the previous experience in the Army is of interest. In World War I, there were 70 cases of tetanus among approximately half a million admissions for wounds and injuries, an incidence of 13.4 per 100,000. In the period between the two world wars there was a similar total number of admissions, with 14 cases of tetanus or 2.4 cases per 100,000. In World War II there were almost three million admissions for wounds and injuries, with a tetanus case rate of only 0.44 per 100,000. Furthermore, a considerable number of cases of serum sickness were undoubtedly prevented through the avoidance of prophylactic antitoxin in the latter period.

The incidence among enemy forces is not entirely known, but from the data that are available the American experience stands out most favorably. For example, it has been reported that there were some 10 cases per 100,000 wounded in the Japanese Army and Navy from 1940 through 1944, a figure comparable with that which occurred among American troops in World War I. Among civilian cas-

ualties during the Manila operations there were almost 500 cases. A report from Europe states that during the Normandy invasion unimmunized German ground forces suffered over 80 cases of tetanus but that there were no such cases in the immunized *Luftwaffe*. There were also 53 cases among American-held German prisoners of war in England during a single month in the latter part of 1944.

The Army report also reviews the civilian mortality from tetanus in the United States and draws attention to the high mortality rate, especially during infancy and early childhood. The civilian mortality rate in young adults during the period of 1936–1938 was calculated as being about twenty times as high as the Army rate in World War II.

From experience gained in the use of tetanus toxoid in the war there is no doubt regarding the efficacy of this procedure for the prevention of tetanus. In military practice reliance was not placed on a continuing state of immunity following immunization; instead, advantage was taken of the rapid rise in blood antitoxin levels that occurs soon after the administration of a stimulating dose of toxoid. Although tetanus is not frequently encountered in civilian practice, it is sufficiently important to warrant active immunization of children and of adults whose activities might lead to injuries potentially infected with *Cl. tetani*. Such persons, when immunized, should be furnished with a record of the procedure so that physicians subsequently treating their injuries may know that the administration of toxoid and not of antitoxin is the treatment of choice.

The Army experience gives no indication concerning the relative efficacy of alum-precipitated toxoid. For children, that agent is thought to be quite satisfactory, particularly since it lends itself well to combination with other antigens, such as diphtheria toxoid. Fluid toxoid, because of its more rapid absorption is considered to be the agent of choice for the booster dose, but there is no good indication that the alum-precipitated material is not just as effective under these circumstances.

In general, it is probably a reasonably safe procedure to give toxoid rather than antitoxin prophylactically to an ex-serviceman who sustains an injury if he states that he was in service for at least a year subsequent to Pearl Harbor and that he received all the routine immunizations administered in his organization. Such a military experience would almost certainly indicate that he had received at least the basic course and would therefore be expected to respond satisfactorily to a stimulating dose of tetanus toxoid.

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GREATER BOSTON NURSING COUNCIL

THERE has been a succession of birthday observances over the years — tercentenaries, sesquicentennials and centenaries — as the settlements and the institutions of our country have paused at various chronologic vantage points to view the achievements of their past. A local youngster now calls attention to the accomplishments of its first decade of life.

The Greater Boston Nursing Council, although organized as the Community Nursing Council on November 17, 1937, had its actual beginning seventeen years earlier in the Committee on Public Health Nursing of the Boston Health League — that uncannily ubiquitous and inclusive organization that, like the news weekly, sees all and hears all. Interested in being sure that all groups in the community had adequate nursing care, the Committee on Public Health Nursing appointed a committee to ascertain the nursing needs in Boston and the community resources to meet these needs. As a result of the recommendations of this committee the Community Nursing Council came into being, becoming in 1942 the Greater Boston Nursing Council for War Service and in 1946 simply the Greater Boston Nursing Council, under which name it now functions.

The activities and the accomplishments of the Nursing Council have already been many as it arrives at its tenth birthday. In the legislative field, with the Massachusetts State Nurses Association, it has been active in promoting legislation to

make mandatory the registration of nurses and to regulate subsidiary workers. In 1942 and 1943 it recruited graduate nurses for the staffing of the proposed Army hotel hospitals, which fortunately were not needed; it did the important work of classifying nurses under the Procurement and Assignment Service of the War Manpower Commission. For nearly five years it has been active in recruiting students for the Greater Boston nursing schools. It has undertaken a number of surveys of nursing services; it has studied nurses' salaries; it is currently sponsoring a committee to consider the matter of experience and observation in public-health nursing for graduate and undergraduate students.

The Nursing Council will continue to have ample opportunity to make its services felt, for the difficulties of supply and demand and the costs in the nursing field continue in an acute phase. We are fortunate in having such an organization ready to do its share in the study of these problems.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR JULY, 1947

RÉSUMÉ

Diseases	July 1947	July 1946	Seven-Year Median
Chancroid	2	2	2*
Chicken pox	664	516	436
Diphtheria	20	31	13
Dog bite	1348	1333	1229
Dysentery, bacillary	11	5	23
German measles	52	133	116
Gonorrhea	352	447	356
Granuloma inguinale	—	1	1*
Lymphogranuloma venereum	—	2	3*
Malaria	15	39	12
Measles	616	2534	1420
Meningitis, meningococcal	8	4	13
Meningitis, Pfeiffer-bacillus	1	2	2
Meningitis, pneumococcal	2	6	3†
Meningitis, staphylococcal	—	—	0†
Meningitis, streptococcal	—	—	0†
Meningitis, other forms	—	—	0†
Meningitis, undetermined	3	8	5†
Mumps	346	216	434
Pneumonia, lobar	107	70	100
Poliomyelitis	21	11	9
Salmonellosis	13	16	11
Scarlet fever	122	179	241
Syphilis	216	486	388
Tuberculosis, pulmonary	251	256	255
Tuberculosis, other forms	13	13	17
Typhoid fever	1	7	4
Undulant fever	6	11	4
Whooping cough	551	562	562

*Three-year median.
†Five-year median.

COMMENT

Diseases above the seven-year median were chicken pox, diphtheria, dog bite, malaria, lobar pneumonia, poliomyelitis, salmonellosis and undulant fever. Chicken pox was at the highest level in the records of the Department.

Diphtheria declined again; there were 20 cases in July compared with 38 and 37 for May and June, respectively.

Poliomyelitis showed the usual seasonal increase, with 21 cases in July whereas only 9 were reported for the preceding six months; 11 were reported in July, 1946.

Diseases below the seven-year median were bacillary dysentery, German measles, gonorrhea, measles, meningococcal and Pfeiffer-bacillus meningitis, mumps, scarlet fever, syphilis, tuberculosis, typhoid fever and whooping cough.

Measles reached the lowest level since 1935, and scarlet fever the lowest in the records of the Department.

GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Diphtheria was reported from: Billerica, 1; Boston, 10; Chelsea, 1; Duxbury, 1; Foxboro, 1; Lynn, 1; Revere, 3; Somerville, 1; Winchendon, 1; total, 20.

Dysentery, bacillary, was reported from: Worcester (State Hospital), 11; total, 11.

Encephalitis, infectious, was reported from: Dover, 1; total, 1.

Lymphocytic choriomeningitis was reported from: Quincy, 1; total, 1.

Malaria was reported from: Barnstable, 1; Boston, 3; Cambridge, 1; Everett, 1; Greenfield, 1; Holbrook, 1; Lynn, 1; Nantucket, 1; New Bedford, 1; North Andover, 1; Waltham, 1; Williamstown, 1; Worcester, 1; total, 15.

Meningitis, meningococcal, was reported from: Boston, 2; Framingham, 1; Lowell, 1; Malden, 1; Montague, 1; Quincy, 1; Waltham, 1; total, 8.

Meningitis, Pfeiffer-bacillus, was reported from: West Springfield, 1; total, 1.

Meningitis, pneumococcal, was reported from: Cambridge, 1; Leominster, 1; total, 2.

Meningitis, undetermined, was reported from: Norwood, 1; Taunton, 1; Ware, 1; total, 3.

Rocky Mountain spotted fever was reported from: Chatham, 1; Dennis, 1; Worcester, 1; total, 3.

Salmonellosis was reported from: Boston, 3; Cambridge, 3; Lawrence, 2; Waltham, 1; Wellesley, 1; Worcester, 3; total, 13.

Septic sore throat was reported from: Boston, 1; North Brookfield, 2; total, 3.

Tetanus was reported from Acton, 1; Attleboro, 1; Hopkinton, 1; Pittsfield, 1; total, 4.

Trichinosis was reported from: Adams, 1; Boston, 1; Fitchburg, 3; total, 5.

Tularemia was reported from Bourne, 2; total, 2.

Typhoid fever was reported from Somerset, 1; total, 1.

Undulant fever was reported from: Ashburnham, 1; Bolton, 1; Holbrook, 1; Warren, 1; Worcester, 2; total, 6.

MISCELLANY

BOSTON UNIVERSITY APPOINTMENTS

Dr. Jacob W. Stutzman, a member of the department of physiology at the University of Wisconsin and for the past two years assistant professor of physiology at that institution, has been appointed associate professor of pharmacology at Boston University School of Medicine.

Dr. Sidney Licht, chief of medical rehabilitation and physical medicine for the Veterans Administration in New England, has been appointed a lecturer in physical medicine at Boston University School of Medicine. Dr. Licht, a resident of Cambridge, formerly taught at Columbia University and at New York University.

CORRESPONDENCE

VACCINATION AGAINST RUBELLA

To the Editor: I have read the comprehensive and critical review of rubella by Dr. Wesselhoeft, which appeared in the June 19 and 26 issues of the *Journal*, with great interest. The recent knowledge of the serious effect on the fetus when this disease is contracted by the mother early in pregnancy, poses new and serious problems from the viewpoint of the health officer. Dr. Wesselhoeft ably discusses the problem of prevention and discards as potentially too dangerous any plan to relax further our isolation practices or to inocu-

late children with rubella virus at an appropriate age. It is my conviction that the practice of inoculation presents less danger of infection of pregnant mothers than the risk that they now run of contracting the disease from contact with unknown and unsuspected cases during epidemics.

German measles is, in its own right, perhaps the mildest of the acute epidemic diseases, and complications, as Dr. Wesselhoeft asserts, are rare. Assuming that technics of artificial inoculation can be worked out to reproduce the disease in its natural or even a milder form, the danger to the child will be no greater than the present risk, or even than the present practice of vaccination against smallpox. Inoculation could be limited to girls but might better include all children. The time and conditions under which the child would be given rubella in private practice could be selected with regard to the known absence of pregnancy in the mother of the family. With pre-school children, knowing the incubation period and the duration of the communicable state, isolation would be relatively easy and reliable. The argument that immunity is not always permanent is valid, but experience shows that second attacks are extremely rare. This practice would protect the next and succeeding generations from the occasional, but dreadful, tragedy of inflicting on their unborn offspring the infirmities of prenatal rubella, as well as saving the mother from the risk of miscarriage.

The proposed program cannot be approached lightly or launched without most careful consideration of all possible contingencies. Our knowledge of artificial inoculation is meager. It should be experimented with, under carefully controlled conditions in institutions, to learn the best means of introducing the virus, the time and duration of the period of communicability and other pertinent details.

Whether adolescent and adult women who have no known history of rubella might be safely inoculated is another question that deserves consideration. With absolute knowledge of the fact that pregnancy does not exist, the proposal does not seem unreasonable.

Although mumps presents an entirely different problem, it may be worthwhile in passing to propose that we encourage exposure of young children to this disease, or practice artificial inoculation. Its consequences in preadolescents are practically nil and complications are exceedingly rare, whereas later in life orchitis in the male may be a serious affair.

I realize that the above proposals are radical and unconventional. As one who has spent much of his life in teaching and in practicing, as a health officer, the prevention of epidemic diseases, it may seem literal heresy. Yet I have observed the futility of our best efforts in attempting to control the acute epidemic diseases of childhood by isolation and quarantine alone. Rubella outbreaks appear, spread and run their course in spite of our efforts. Now that we are confronted with a hitherto unsuspected danger to life and health from this disease, even if only rarely when we have the simultaneous occurrence of early pregnancy and rubella, I believe that the public-health profession should study every possibility to prevent this event. The above proposal is at least worth further study and consideration.

C. M. Hilliard
Simmons College
Boston

* * *

Professor Hilliard's letter was referred to Dr. Wesselhoeft, whose reply is as follows:

To the Editor: The suggestion contained in Professor Hilliard's communication is a consummation devoutly to be wished, but there are difficulties in bringing it about, which were presented in my progress review on rubella. It is not an easy matter to cultivate the virus of rubella, and, furthermore, the inoculation of such material does not ensure a successful take. Until a more successful method of cultivation of the virus is achieved than has been accomplished up to the present, inoculation cannot be considered a practical procedure.

I am heartily in agreement with Professor Hilliard that every effort should be made to perfect a satisfactory vaccine against rubella. Without such a vaccine, it is well to keep in mind the problems that I attempted to set forth under the heading "Prevention."

Conrad Wesselhoeft, M.D.
315 Marlboro Street
Boston

BOOK REVIEWS

Treponematosis. By Ellis Heradon Hudson. 4°, paper, 122 pp. New York: Oxford University Press, 1946. Reprinted from *Oxford Medicine*.

This book constitutes a new and important interpretation of available evidence regarding the relation between the various maladies produced by treponemas. The evidence considered embraces the historical, clinical, pathological, immunologic and epidemiologic aspects of the question. The facts have been marshaled logically and presented clearly and unemotionally.

The essential conclusions are that, at present, there is no justification for regarding *Treponema pertenue* of yaws and *T. carateum* of pinta as valid species; that syphilis, yaws, pinta, bejel and other so-called "syphiloids" are all caused by *T. pallidum*; and that the maladies named should be regarded as different patterns or syndromes of a disease that is fundamentally the same. Hudson recognizes that the differences between yaws and syphilis are often but not always so pronounced that a layman can distinguish them readily, and he favors retention of the accepted names for the various clinical entities or syndromes caused by treponemas.

The reviewer accepts the conclusions and believes that physicians who are interested in any form of treponematosis will wish to read Hudson's presentation of the subject.

The Ego and the Mechanisms of Defense. By Anna Freud. Translated from the German by Cecil Baines. 12°, cloth, 196 pp. New York: International Universities Press, Incorporated, 1946. $4.00.

It must be stated at the outset that this small book will not be understood by the uninitiate or neophyte in psychiatry, particularly by those without a goodly quantity of psychoanalytic exposure. The text starts with what has been controversial in previous considerations of the functions and constituents of the ego. Then, chapter by chapter, attempts are made to depict the ego in the light of its defenses against many awe-inspiring opponents. This process of construction is carried on — as in many psychoanalytic presentations — as though the ego, id and superego were as tangible and discrete "psychic institutions" as they seem to the analysts. The various well known ego defenses from instinctual "invasions" and superego attrition are described, but with relatively little illustrative case material.

In many sections of the text the discussions point out so many controversial issues that the reader receives an impression of being in the midst of an informal psychoanalytic society subcommittee meeting whose chairman is proposing or dispensing with classifications. An example is the following quotation (Chapter IV):

> According to the English School of analysis, introjection and projection, which in view should be assigned to the period after the ego has been differentiated from the outside world, are the very processes by which the structure of the ego is developed and but for which differentiation would never have taken place . . . the chronology of psychic processes is still one of the most obscure fields of analytic theory. . . . It will probably be best to abandon the attempt so to classify them and, instead, to study in detail the situations which call forth the defensive reactions.

To the reviewer, there did not appear to be any clear differentiation between anxiety and affect against which the ego must defend itself. Nor were the superego and the parental prohibitions against which the child may not transgress differentiated — childhood neurosis thus being arbitrarily separated from adult neurosis. In other sections the discussion did not distinguish between childhood and adult affect and anxiety.

Quite properly, the author stated (perhaps not emphatically enough) that the revelation of ego defenses makes the latter inoperative and may weaken the ego so as to advance a pathologic process.

The tried-and-tested case of Little Hans was again used to illustrate aggressive drives, resulting fears and genitalized fantasies — this time as ego defenses. Interesting deductive analyses of animal and circus fantasies and childhood stories are given as phases of the infantile(?) ego. These were

related to productive symptoms in the adult psychotic patient. It was also pointed out that parents frequently encourage escapes from reality in their children by inducing fantasies and adult impersonations of pleasurable type; the criteria of acceptance for these are then proportional to the conspicuousness of the symbols employed.

Interesting examples of reversal of aggression anxiety were given to illustrate identifications with the aggressor as developmental in superego formation.

The phenomena at puberty were related to those occurring in infantile and involutional eras in a brief space (Chapter XI). Here the ego was again described as being rendered *hors de combat* between the immutable id and the inevitable superego, the result being the liberation of genital territory or its control by both ego and superego.

A brief discrete attempt was finally made to differentiate normal from pathologic features of ego defenses during puberty. The answer was qualified with provisos. The concluding chapter extols the ego by the magnitude of its defenses.

By an unusual amount of scrutiny the reviewer found many novel and useful items in this book. This may be possible for others quite well versed in analytic terminology. For those not so prepared the efforts necessary to learn from this text may outweigh its usefulness.

Gastroenterology in General Practice. By Louis Pelner, M.D. With the collaboration of Louis A. Held, M.D., and contributions from Alexander Lewitan, M.D., Samuel Waldman, M.D., and Siegfried W. Westing. 8°, cloth, 285 pp., with 108 illustrations and 15 tables. Springfield, Illinois: Charles C Thomas, 1946. $7.50.

This book is designed for the busy practitioner and medical student. It will not appeal to the expert in gastroenterology. It is planned as an everyday handbook rather than a complete reference work and contains much useful information, well classified and clearly presented, with rarely an opinion that can be questioned. It attempts to cover the whole subject of gastroenterology in about two hundred and sixty pages, including pathology, symptoms, physical examination, laboratory tests in detail and treatment, with the result that it presents rather brief pictures of some important subjects, such as the surgical treatment of bleeding ulcer and pyloric obstruction and the medical treatment of gastritis. Only two diseases of the liver are described in detail — portal cirrhosis and cholecystitis. Less frequent conditions, such as tumors of the liver and polyps and diverticulums of the stomach and duodenum, are omitted; the importance of prepyloric ulcer in the stomach is not mentioned.

Tables of differential diagnosis and diets are freely used, and the book is fully illustrated with roentgenograms that, for the most part, are excellent. About two thirds of the book consists of text, and about a third of illustrations, tables and diet lists. It is possible that the use of tables is somewhat overdone.

The arrangement of chapters is unusual. The work begins with history taking, and one proceeds two thirds through the book before simple laboratory methods are reached. It would seem simpler to put all the diseases of the bowel together, and diseases of the liver and gall bladder in sequence. The author does well to limit the liver-function tests to thirteen or fourteen instead of the twenty to fifty that are sometimes mentioned. It is unfortunate that he has not included two of the simplest and best and most modern tests — the thymol-turbidity test of the blood serum and the Harrison spot test for bilirubin in the urine.

Functional diseases of the gastrointestinal tract are mentioned throughout the volume. At the end of the book there are two excellent chapters — one on psychosomatic symptoms in gastrointestinal disease and the other on simple methods of treatment that the general practitioner can use.

The type, paper and index are excellent.

The Anatomy of the Bronchial Tree: With special reference to the surgery of lung abscess. By R. C. Brock, M.S. (Lond.), F.R.C.S. (Eng.). 8°, cloth, 96 pp., with 142 illustrations. New York: Oxford University Press, 1946. $12.00.

The author of this book successfully justifies his criticism that the qualified physician has not yet learned to approach the diseases of the lungs from the point of view of the segmental distribution of the bronchi. Only such knowledge will, he contends, enable a surgeon adequately to deal with conditions such as septic pneumonitis and lung abscess. This is a stimulatingly instructive book. The exceptionally clear photographs — in color and in black and white — of metallic casts of the bronchial tree, made with the lungs in situ, the accurate drawings, and the clear bronchograms, both normal and abnormal, give considerable support to this point of view. This book deals with bronchial embolism and posture in relation to lung abscess, the level of the interlobar fissures of the lungs, the right upper lobe, the left upper lobe, the middle lobe, the lower lobes and the whole lung (anomalies and compound abscesses). The reviewer finds this book useful and provocative. The author's scholarly approach in presenting the material should place all physicians and surgeons in his debt. There can be no question that this book should be on the shelves of every medical-school and hospital library and in the personal libraries of those concerned with diseases of the chest.

An Integrated Practice of Medicine. By Harold T. Hyman, M.D. Four volumes and index volume. 8°, cloth, 4141 pp., with 1184 illustrations (305 in color) and 319 diagnostic tables. Philadelphia: W. B. Saunders Company, 1946. $50.00.

This is an unusual system of medicine. Compiled largely by one writer, it comprises four large volumes and contains many millions of words. The task of putting it together must have been prodigious.

The author wished to supply the general practitioner with a modern handbook that would deal with all phases of modern medical work. No barriers of specialty practice have been permitted to obstruct the landscape. A pregnant mother or a patient with appendicitis, tuberculosis or any other ailment needs competent medical advice, and how to give this is described.

Clearly, it is impossible for any reviewer to do more than nibble at the various chapters in a work of such magnitude. This particular reviewer has enjoyed his acquaintance with the book as obtained in this manner. He believes that the thousands of physicians for whom it was written will like it, will learn much from it and will be grateful to the author.

Your Rheumatism and Backaches. By Joseph D. Wassersug, M.D. 8°, cloth, 254 pp. New York: Wilfred Funk, Incorporated, 1947. $2.50.

This book is written to give the layman insight into the causes and treatments of symptoms and signs that are commonly labeled rheumatism or backache. It is a worthwhile endeavor for the occasional intelligent patient who requests further information to understand and follow treatment more effectively.

It is far more difficult to write a helpful and readable book for the laity than to write one for physicians. Most books of this type are written by men of wide clinical experience and deep understanding of the patient's problem. Because the author is a young man, a number of minor faults must be overlooked in this book. In later editions, less quoting from the writings of other men and a more critical analysis of the effectiveness of the treatments described, with illustrations drawn from the author's own experience, may be expected. An important omission — the most important in health education — is the absence of any discussion of preventive measures that the patient may apply. Many insurance companies, as well as a number of physicians, have attempted discussions of the public-health aspects of these conditions.

The material comprising this book is well arranged. It is written in an interesting, readable style. It should be a helpful book for the lay reader.

Parenteral Alimentations in Surgery: With special reference to proteins and amino acids. By Robert Elman, M.D. 8°, cloth, 284 pp., with 31 figures and 21 tables. New York: Paul B. Hoeber, Incorporated, 1946. $4.50.

The frontiers of surgery were long restrained by a lack of appreciation of the significance of water, electrolyte and protein requirements in patients subjected to operation. During the past half century a body of knowledge regarding

these needs and their fulfillment has accumulated. The clinical application of this information has contributed materially to the dramatic expanse of surgical endeavor and to the significant reduction in mortality and morbidity of major surgical procedures.

This text is a comprehensive discussion of the evolution of this phase of therapeutics by an authority whose original contributions to the development of parenteral protein alimentation have been outstanding. It deals adequately with the biochemical basis of nutritional requirements, as well as with the technical methods of their accomplishment by parenteral means.

Cardiovascular Diseases. By David Scherf, M.D., and Linn J. Boyd, M.D. Second edition. 4°, cloth, 478 pp., with 56 illustrations. Philadelphia: J. B. Lippincott Company, 1946. $10.00.

This deservedly popular text has been improved by the inclusion of important new material. In particular, a reasonably adequate treatment of the subject of rheumatic fever eliminates a serious omission in previous editions. The authors continue to pivot their discussion of diseases of the heart around specific structural abnormalities rather than etiologic factors. For instance, tricuspid stenosis, tricuspid regurgitation, mitral stenosis and mitral regurgitation are taken up as individual entities without emphasis on their common rheumatic origin. Although space is given to consideration of rare types of myocarditis, one looks in vain for mention of the important role that the myocardial lesion plays in the cardiac failure of chronic rheumatic valvular disease.

The book gives the impression of having been compiled from a series of lectures — each complete and excellent in itself but the whole lacking somewhat in integration. A good bibliography is appended to each chapter.

Allergy in Theory and Practice. By Robert A. Cooke, M.D., Sc.D. In association with Horace S. Baldwin and others. 8°, cloth, 572 pp., with 1 color plate. Philadelphia: W. B. Saunders Company, 1946. $8.00.

Each year the American College of Physicians sponsors a variety of postgraduate courses, and one of the most popular has always been that on allergy directed by Dr. Robert A. Cooke, of New York City. This volume is a written account of the teaching to which his pupils have been thus exposed.

The book is excellent — a collaborative enterprise that ties together a vast amount of allergic information. Dr. Cooke, as leader, has written several chapters, including one on medical education and allergy that gives his ideas on so broad a problem with both clarity and brevity. The ordinary aspects of allergy are discussed by others of the team, who are experts not only as clinicians but also as investigators and teachers.

Although most of the subjects that come under discussion are clinical in nature, the basic sciences on which allergy is founded are not forgotten. Hence, the topics of chemistry, pathology and immunology receive due consideration. At the end of almost every chapter is a concise bibliography, so that any student who wishes to dig more deeply into any phase of allergy receives good directions.

On the whole, this textbook is certain to be successful. All students, whether they are undergraduates or postgraduates, practitioners or specialists, will wish to study it. It is recommended wholeheartedly.

Uterine Contractibility in Pregnancy: A study of the contractions of pregnancy and labor under normal and experimental conditions. By Douglas P. Murphy, M.D. 4°, cloth, 134 pp., with 64 illustrations. Philadelphia: J. B. Lippincott Company, 1946. $5.00.

The Larand tocograph is an instrument that, when strapped to the abdomen of a pregnant woman, records by means of a pen writing on a moving strip of paper the frequency and amplitude of uterine contractions, as well as the degree of uterine tone. With this device Murphy has made three thousand, one hundred and fifty-four observations on 1153 subjects and has arrived at the following conclusions: the character of uterine contractions varies in different persons; the characteristic contractions of a given patient follow a distinctive pattern throughout pregnancy and labor; the first significant rise in uterine activity may be detected in the average woman at about the twenty-first week of pregnancy; and there is a period of relative quiescence up to the thirty-fourth week, one of nonrhythmic activity from the thirty-fifth to the thirty-eighth week and a final period of rhythmic activity in the last two weeks.

Murphy believes that if a subject exhibits uterine motility in early pregnancy or a high degree of rhymicity during pregnancy she will manifest a satisfactory quality of uterine motility during labor. Inertia, according to the author, more frequently follows a poor pattern of contraction than an unsatisfactory quality of activity.

In the treatment of inertia Murphy states that pituitary extract may be used safely in the absence of fetopelvic disproportion if there is no excessive elevation of uterine tone as revealed by the tocograph.

Murphy's work with the tocograph is a distinct contribution toward the study of the physiology of pregnancy and labor. Its value, however, would have been enhanced if he had made more consecutive observations during both pregnancy and labor on a large number of patients. Moreover, from the practical point of view, much of the information furnished by the instrument can be obtained by the trained hand of the experienced obstetrician.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Nutritional and Vitamin Therapy in General Practice. By Edgar S. Gordon, M.D., Ph.D., associate professor of medicine, University of Wisconsin Medical School. Third edition. 8°, cloth, 410 pp., with 47 figures and 23 tables. Chicago: Year Book Publishers, Incorporated, 1947. $5.00.

The author published the first edition of this book in 1940 jointly with E. R. Sevringhaus, and this third edition has been revised to include the new information in the literature since 1942. The volume includes material on dental problems in nutrition and on the economic side of clinical nutrition, as well as valuable tables on market lists for meals of low and moderate cost and on the nutritive values of selected foods. An appendix lists commercial vitamin preparations. A good index completes the volume, which is well printed with a good type on light soft paper that is pleasing to the eye. It is worthy of note that the standard of medical-book publication is steadily increasing in the post-war era.

Milk and Food Sanitation Practice. By H. S. Adams, B.S., chief, Bureau of Environmental Hygiene, Division of Public Health, Minneapolis, and lecturer, School of Public Health, University of Minnesota. 8°, cloth, 301 pp., with 65 illustrations. New York: The Commonwealth Fund, 1947. $3.25.

This textbook is written for students of public health and workers in health departments who have charge of the sanitary control of milk and food supplies. The place of education in the sanitation program is stressed. The text is divided into two main divisions: milk sanitation and food sanitation. Each division has a bibliography of selected references. A chapter is devoted to a short history of milk control, with a full discussion of the severe epidemic of septic sore throat traceable to the use of raw milk in Lee, Massachusetts, in 1928. The following chapters consider the milk-control program, the essentials of sanitary milk production, the various aspects of pasteurization, laboratory procedures used to evaluate milk supply and the sanitary control of frozen desserts. The food division is in three parts: the food-control problem, with a discussion of federal, state and local inspection; essentials of food-establishment sanitation; and the instruction and training of food handlers. Eleven appendixes are devoted to important supplementary information, among which may be mentioned essential and special food field equipment, food poisoning and infections, courses for the instruction of food handlers, the use of DDT as an in-

secticide and a list of films relating to milk and food sanitation. The material is well organized, the text well written, and the volume well published in every way. The book is recommended for all medical, public-health and public libraries and should prove valuable to all persons interested in the subject.

Penicillin Therapy, including Streptomycin, Tyrothricin and Other Antibiotic Therapy. By John A. Kolmer, M.D., Dr.P.H., Sc.D., LL.D., L.H.D. Second edition. 8°, cloth, 339 pp., with 27 illustrations and 37 tables. New York: D. Appleton-Century Company, 1947. $6.00.

This new edition has been largely revised and in part rewritten, and it has been enlarged by the addition of new material. New chapters have been added on the antibiotic agents other than penicillin and on antibiotic therapy in relation to veterinary medicine. In the first edition the clinical use of antibiotic agents in the treatment of various diseases was discussed from the standpoint of etiology, but in this edition the subject is discussed under pathologic entities. It is hoped that this arrangement will prove more valuable to clinicians. A long list of selected references is appended to each chapter. The volume is well printed with a good type on good paper and is recommended as a reference source for medical libraries and physicians.

Parergon. Third edition. Fo. paper, 208 pp. Evansville, Indiana: Mead Johnson and Company, 1947. $5.00.

This edition reproduces the art of American physicians in various mediums. Two hundred and five pages are devoted to reproductions of the work. The quality is high, and some of the work is of a professional standard. There is a feature article on physicians as artists. The front cover is devoted to panels depicting Apollo, Aesculapius and Hygeia, and the back cover illustrates the restoration of the temple of Aesculapius at Epidauros. A number of Boston and Massachusetts physicians are represented in the selections. An index of artists is included in the volume. This book should be owned by every physician interested in the fine arts and should be in the historical collections of all medical libraries.

The Pharmacopoeia of the United States of America. By authority of the United States Pharmacopoeial Convention, Washington, 1940. Thirteenth revision (U.S.P. XIII). 8°, cloth, 957 pp. Easton, Pa., Mack Publishing Company, 1947. $8.00.

This revision is official from April 1, 1947. In the compilation of this edition the contents have been restricted to substances that reflect the best state of the medical knowledge of today and to preparations that may be most efficiently administered or used. For the first time English titles are given first, followed by the Latin equivalents. The revision of the *Pharmacopoeia* is continuous, and from time to time supplements listing new admissions are published. The excellence of publication has been maintained despite current difficulties. This standard reference work should be in all medical libraries.

Studies from the Rockefeller Institute for Medical Research. Reprints. Vol. 130. 8°, paper, 666 pp. New York: The Institute, 1947. $2.00.

This volume is made up of reprints of articles originally published in various periodicals during the last part of 1946 and brought together in one volume for convenient reference. The articles have been repaged consecutively, and an author and a subject index supplied.

Physician's Handbook. By John Warkentin, Ph.D., M.D.; and Jack D. Lange, M.S., M.D. Fourth edition. 12°, paper, 282 pp. Chicago: University Medical Publishers, 1946. $1.50.

This pocket manual, first published in 1941, has been revised to include new material that has appeared since the publication of the last edition in 1944. The scope of the book has been extended to serve as a ready reference source for many types of medical and dental practice, and to include a relatively complete laboratory manual. Its popularity and usefulness are attested by the need of four editions in six years.

Tuberculosis: As it comes and goes. By Edward W. Hayes, M.D., associate professor of tuberculosis, College of Medical Evangelists, Los Angeles, member of the attending staff, Los Angeles County Hospital, Division of Tuberculosis, director of tuberculosis, Imperial County, California, and medical director and physician-in-charge, Maryknoll Sisters Sanatorium, Keane Sanatorium and Lair Sanatorium, Monrovia, California. With chapters by Laurence de Rycke, Ph.D. Second edition. 8°, cloth, 220 pp., with 92 illustrations. Springfield, Illinois: Charles C Thomas, 1947. $3.75.

This popular manual designed for the sufferer from pulmonary tuberculosis is written in plain, nontechnical language and discusses the cause and nature of the disease and its treatment. The material is well organized and the chapters on classification and mechanical therapy are well illustrated with sketches from x-ray films. The short chapter on history could have been omitted without detracting from the value of the manual. The short quotation "Tuberculosis is as old as mankind" would be sufficient for a book of this type and would carry more weight than the sketchy history. De Rycke has written two important chapters on suggestions to patients and to visitors. The text is printed with a beautiful, clear, large type on good paper, a delight to weary eyes. The book should prove useful to patients as well as to physicians interested in pulmonary tuberculosis. It is recommended for public and medical libraries.

Aging Successfully. By George Lawton, M.D. 8°, cloth, 266 pp. New York: Columbia University Press, 1946. $2.75.

This is a book for the layman and is not intended for the student or practitioner of geriatrics. It is written in an easy narrative style and covers the problems of advancing age in its many aspects. Dr. Lawton believes that the best time to prepare for old age is in childhood but that it is never too late to begin, although the task becomes increasingly difficult with the advancing years. To grow old successfully requires individual thought and effort. There is nothing that can completely erase illness, infirmity, poverty, loneliness, frustration and disaster. Of particular interest are the chapters on jobs after fifty, retirement, love at maturity, relations with younger persons and the philosophy of the aged. The author stresses the need of retiring to an occupation or vocation. He discusses frankly and soundly the love relations of old and young persons. Interspersed throughout the text are many stories pertinent to the problems under discussion. The reviewer, being technically near old age, is favorably impressed by the soundness of the advice and suggestions given by Dr. Lawton and by his analysis of the problems confronting the aging person in various situations. This book should be in all libraries, both general and medical, and can be read with profit by young and old of both sexes.

NOTICES

VAN METER PRIZE AWARD

The American Association for the Study of Goiter again offers the Van Meter Prize Award of three hundred dollars and two honorable mentions for the best essays submitted concerning original work on problems related to the thyroid gland. Provided essays of sufficient merit are presented in competition, the award will be made at the annual meeting of the association, which will be held in Toronto, Canada, on May 6, 7 and 8, 1948.

The competing essays may cover either clinical or research investigations, should not exceed three thousand words in length and must be presented in English; a typewritten double-spaced copy should be sent to the corresponding secretary, Dr. T. C. Davison, 207 Doctors' Building, Atlanta 3, Georgia, not later than February 1, 1948.

A place will be reserved on the program of the annual meeting for presentation of the winning essay by the author if it is possible for him to attend. The essay will be published in the annual *Proceedings* of the association. This will not prevent its further publication, however, in any journal selected by the author.

(*Notices continued on page xv*)